Patterns of fatigue in patients receiving chemotherapy.

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Patterns of Fatigue in Patients Receiving Chemotherapy

by

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ABSTRACT

Fatigue is reported to be a significant and distressing problem for people receiving chemotherapy, but the phenomenon of fatigue is poorly understood and little is known about the factors influencing it. Nurses need to understand the parameters of fatigue in order to effectively help the individuals with cancer who experience it.

The first aim of this study was to chart prospectively onset, pattern, duration, intensity and distress associated with fatigue in people receiving chemotherapy alongside associated self-care actions initiated in response to this symptom. A second aim was to identify whether such factors as: age; type and stage of disease; type, pattern and nature of chemotherapy; mood and symptom distress were associated with the occurrence of fatigue. Data were collected from one hundred and nine patients receiving different chemotherapy protocols. Data collection tools included daily patient-kept diaries, the Mood Adjective Checklist, the Holmes Symptom Distress Scale plus semi-structured interviews.

A quantitative approach was taken to analysing the continuous stream of daily data and the repeated measures at scheduled intervals, including time series analysis and descriptive statistics. Visual and statistical analyses revealed patterns of fatigue. Mean fatigue scores were significantly greater for patients with cancer of the pancreas and breast than those with a small cell lung or ovarian cancer . Certain chemotherapy protocols and the manner in which the drugs were administered also appeared to influence fatigue. Mood and symptom distress scores were moderately to strongly correlated with the dimensions of fatigue. Subjects performed a variety of different self-care behaviours, and these were most frequently concerned with modifying or altering activity and rest patterns and employing psychological strategies. Findings indicate that, although overall fatigue may be similar between chemotherapy groups, there is considerable individual variation in the extent of fatigue and the amount of associated distress.

These findings have important implications for clinical nurses planning the care of patients undergoing chemotherapy. Furthermore this study raises important methodological issues for consideration in future research.

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CHAPTER 1

INTRODUCTION

Fatigue is seldom regarded as a serious problem by healthy people because it is usually a temporary phenomenon. In contrast, for those with a chronic illness such as cancer, the cause of fatigue may not be readily apparent. It is not relieved by sleep and may be persistent. Dealing with the symptoms of illness and its treatment, such as fatigue, pain and nausea become a challenge, which patients and their families require help to meet successfully.

Fatigue is often recognised as the most frequently reported symptom of cancer and cancer treatment. Individuals with cancer may experience fatigue as a result of the disease, as a side effect of treatment, and as a result of the psychological distress generated through the diagnosis (Aistars, 1987). The incidence of fatigue reported by cancer patients treated with radiotherapy, chemotherapy and biological therapy reaches 90% (Haylock and Hart, 1979 [radiotherapy]; Nerenz, Leventhal and Love, 1982 [chemotherapy]; Quesada, Talpaz and Rios, 1986 [Interferon]). Fatigue has important implications for cancer care. Patients may discontinue treatment, and doses of treatment may be limited. From the patient's perspective fatigue has been reported as the most disturbing symptom experienced during treatment (Rhodes, Watson and Hanson, 1988) with the greatest potential to interfere with self-care (Fernsler, 1986). Quality of life is affected profoundly as the ability to perform household tasks and enjoy leisure activities becomes disrupted (Todres and Wojtuik, 1979), leading to impaired self concept when roles and relationships are changed (Aistars, 1987). Despite recognition of its prevalence among patients with cancer and the extent to which it can interfere with daily activities, there is limited research describing the time of onset, duration, pattern or severity of fatigue, identification of contributory factors or interventions designed to prevent or ameliorate it.

The need for research into the phenomenon of fatigue in cancer patients is indicated for several reasons. Firstly, it could provide insight into the reactions of patients to cancer and cancer treatment which result in fatigue. Secondly, information gained on the subjective dimensions of fatigue could be used in the process of patient education. Finally, the development and testing of realistic interventions for this problem could enhance supportive care.

This study developed from the author's previous work with cancer patients in relation to the self-care management of nausea and vomiting (Richardson, 1994). This small scale study explored the nature, number and perceived effectiveness of self-care behaviours, and recorded the frequency, intensity and distress associated with nausea and vomiting resulting from chemotherapy. Further the relationship between nausea and vomiting and the performance of self-care was described. Whilst reviewing the literature concerned with patients' symptoms arising as a consequence of cancer treatment, the author was impressed by the frequency with which fatigue was mentioned as one of the most distressing symptoms in this population and also by the apparent lack of any further detailed literature.

Hence, the design of the present study was developed with the express purpose of monitoring the subjective dimensions of fatigue in a sample of cancer patients who were receiving chemotherapy principally with the use of a daily diary designed by the researcher. It aimed to provide a description of the relationships of a number of factors, such as alterations in mood state and the degree of symptom distress which have been postulated within the empirical and anecdotal literature to influence this phenomenon. It was planned to document the nature of any self-care behaviours utilised by patients in response to fatigue and the perceived effectiveness of these measures. This study sought to develop both the theoretical and clinical knowledge base concerned with patients' experiences of dealing with fatigue which results from the administration of chemotherapy. Hegyvary (1993) addresses questions concerned with the development of the knowledge base for nursing practice with particular regard to managing patients' symptoms effectively. She considers that for two reasons research into the management of symptoms is an essential adjunct to research about disease and treatment. First, symptoms usually are manifestations of disease processes, which people have to live with, both before and during successful treatment. Second, the successful treatment of many diseases may not lead to the abatement of symptoms, as some become chronic, such as fatigue, even when the disease process is brought under control. This common occurrence adds emphasis to the need for research to define and measure patient symptoms such as fatigue, and to test effective approaches to their management. This study of fatigue in cancer patients was designed with the former of these ends in view.

The use of time-series designs in both experimental and descriptive research is acknowledged as uncommon (Clinton, 1986). But, in practice, nurses are involved in periodic monitoring of multiple factors in the same patient. At the descriptive level it is critical that, as the domains of fatigue are described and measured, there is also systematic generation of knowledge about whether and how the phenomenon of fatigue

naturally fluctuates over time in different populations of cancer patients. There is a desire for nurse researchers to investigate clinical phenomena and the processes that surround them, and time-series designs have been acknowledged as being particularly well-suited for research into varied aspects of contemporary nursing practice. The substance of this study is concerned with an attempt to document both the pattern and relationships of fatigue to other factors, in patients receiving a variety of chemotherapy regimes, over the time period of one pulse of chemotherapy. The utility of a number of analysis strategies are explored in order to obtain an accurate picture from the data.

This thesis is organised to reflect the process of conducting the research. Chapter 1 introduces the study, its origins, purpose and significance for cancer nursing. The literature review is divided into three chapters. Chapter 2 reviews the literature on fatigue in health and illness, and includes a historical overview of the study of this subject across a variety of disciplines, including nursing. Chapter 3 provides an account of the differing methods which have been adopted to measure fatigue within the literature, in particular self-report measures. In Chapter 4 a review of the research literature concerning fatigue in cancer patients is presented, evaluating the quality of the evidence, thus helping to focus the direction and methodological rigour required in the present study.

Next the methods are considered. Chapter 5 provides a theoretical account and rationale for the choice of study methods and describes how the study was conducted: the selection and refinement of methods employed to collect the data through a series of pre-tests and a pilot study, the organisation of data collection, and the strategies adopted for analysis of the two discrete time streams: (a) the continuous stream of daily data, and (b) the repeated measures at scheduled intervals.

The results are presented in three chapters. Chapters 6, 7 and 8 present the results of the study. Chapter 6 introduces the properties of the sample and the type of data obtained, this is followed by a description of the pattern of change in fatigue using a number of different approaches. Chapter 7 details the results of the analysis concerned with the aggregated data set. Chapter 8 concludes this section of the thesis with details of the results concerned with the analysis of data collected at spaced intervals and the findings from the variety of procedures concerned with exploring the validity and internal consistency of the selected instruments.

Chapter 9 discusses the findings from the study in relation to previous empirical knowledge and theory, detailing the limitations inherent in the design chosen and the selected methods of data collection. Finally, Chapter 10 concludes the thesis with an examination of the research avenues open to researchers when examining this

phenomenon and the implications of the findings of the present study for cancer nursing practice.

The significance of this study lies in its contribution to the emerging body of knowledge concerned with the phenomenon of fatigue and its measurement, particularly in patients with cancer. In particular the adoption of a variety of visual and statistical methods confirmed the profound daily variation in fatigue including the other symptoms and mood states that cancer patients receiving chemotherapy experience. Insights gained during this study about the likely pattern of fatigue in the period following the administration of chemotherapy may be utilised by nurses engaged in the care of chemotherapy patients. The provision of accurate information on the likelihood of experiencing fatigue, its duration and probable relation to other symptoms the patient may experience could form a vital part in any information programme designed for chemotherapy patients. The nature of self-care behaviours found beneficial by this group of patients should be made known to patients and their families. Nurses should actively involve themselves in the support of patients who wish to use self-care strategies in the amelioration of this symptom, particularly patients may require assistance in the development of a realistic timetable for activity and rest which acknowledges the importance of maintaining cherished activities.

Research with cancer patients is often challenging due to the need to obtain information at a time when patients are most likely to be under stress and particularly sensitive to questions relating to illness and its treatment. It is clear that often the most theoretically interesting questions of relevance to the practitioner rely on data that are difficult to collect. Methods to address theoretically interesting and clinically perplexing issues often strike emotionally distressed cancer patients as tangential to their immediate needs and experiences. The design and conduct of this particular piece of clinical research evolved in the face of such challenges.

CHAPTER 2

FATIGUE IN HEALTH AND ILLNESS

2.1 Introduction

Fatigue is a common symptom experienced by most people at some time. Usually it occurs either after exertion, with illness, or accompanies psychological stress/crisis. Fatigue can be a normal and expected response, or it can be disproportionate and acquire serious significance for an otherwise healthy individual, becoming a principal limiting factor for which they seek care (Kellum, 1985). Hence, fatigue is a symptom of abnormality when it becomes the occasion for complaint, because it results from less effort than is customary, at unusual times, or when rest is no longer recuperative or diversion is not distracting (Engle, 1970). Such fatigue is debilitating, persisting over time and interfering with daily life (Potempa, Lopez, Reid and Lawson, 1986). When it becomes unusual, excessive, or constant it serves as the first indicator of disease. Fatigue is probably the most prevalent symptom of mental and physical illness.

Although fatigue is a common experience and is understood to mean that the person is tired and unable to continue, helping the person with fatigue can be complicated and difficult. Patients do not mention fatigue unless it is a prominent symptom, impedes their lives, or they are specifically asked (Hart, Freel and Milde, 1990). The anticipation of fatigue tends to reduce its importance to care providers and often to the patient, who hesitates to report anything so commonplace (Morris, 1982). Yet it can be a distressing symptom, affecting performance and the image of self as a capable, functioning person. Because many people look to health care providers for an explanation of their fatigue and ways to handle it, it is necessary that nurses have a thorough understanding of the symptom.

2.2 Scope Of The Review

The review contained in Chapter 2, 3 and 4 will discuss empirical work and literature pertaining to the concept of fatigue, with particular reference to cancer. The research studies and material for the review span the years 1970 to the present, although including what are considered seminal contributions prior to 1970. This period was selected as

earlier research and contributions on the subject by nurses were not evident. Material was identified through both primary and secondary channels including all major nursing bibliographies, abstracting journals and indexing journals, and computer assisted information retrieval services, with special reference to the Cumulative Index To Nursing And Allied Health Professional Literature, Medline and Cancerlit.

The review focuses on nursing research concerned with fatigue. However, the material concerned with fatigue and work, the physiological basis of fatigue, exercise physiology/sport and chronic fatigue syndrome is not exhaustive. The work reviewed in these areas is by no means representative of the studies on these topics, but has been selected as it illustrates relevant theoretical and clinical issues, and details the thoughts of scientists who have been influential in this field and consequently shaped the present theoretical and empirical orientation in nursing.

2.3 Historical Overview

Study of fatigue has interested many different groups. Understanding fatigue is, for example, of practical concern to industry. Substantial contributions in this area have centred on fatigue and poor performance and the relationship of the work environment to this phenomenon. The focus of such research is concerned with maximising productivity with appropriate work schedules and developing an environment least likely to promote the deleterious effects of fatigue. A second group, researchers investigating the effect of flight, are interested in fatigue because safe, efficient and effective functioning of pilots and crew members depends on understanding this phenomenon. Workers in this area have examined the cumulative effect of prolonged stress and mental effort on skills. A third group with long-standing interest in fatigue is involved in the pursuit of athletic excellence, where winners are those who become fatigued last. Early workers were primarily concerned with the effect of muscular work on fatigue of nerve fibres. Medical interest in the phenomenon is stimulated because it is argued that fatigue is probably the most prevalent symptom and often the first indication of both physical and mental illness (Minden and Reich, 1983).

Nurses first began to investigate fatigue in 1972 when Hart (1978) compared fatigue patterns in multiple sclerosis (MS) patients and healthy controls. Hart later collaborated with Freel to identify indicators of fatigue in MS patients (Freel and Hart, 1977), and with Haylock to identify fatigue indicators in radiation therapy patients (Haylock and Hart, 1979). The number of nursing studies increased dramatically in the 1980's (Davis, 1984 ; Potempa, Lopez, Reid *et al.*, 1986 ; Rieger, 1987). Several factors contributed to this

surge in nursing research. Key publications summarising the fatigue literature made it easier for nurses new to this body of knowledge to master its complexities quickly (Norris, 1982 ; Atkinson, 1985 ; Kellum, 1985 ; Valdini, 1985 ; Varricchio, 1985 ; Potempa, Lopez, Reid *et al.*, 1986 ; Piper, Lindsey and Dodd, 1987). Fatigue became

Figure 2.1 North American Nursing Diagnosis Association - nursing diagnosis for fatigue

DEFINITION

An overwhelming sustained sense of exhaustion and decreased capacity for physical and mental work.

DEFINING CHARACTERISTICS

Major : verbalisation of an unremitting and overwhelming lack of energy; inability to maintain usual routines.

Minor : perceived need for additional energy to accomplish routine tasks; increase in physical complaints; emotionally labile or irritable; impaired ability to concentrate; decreased performance; lethargic or listless; disinterest in surroundings/introspection; decreased libido; accident prone.

RELATED FACTORS

Decreased/increased metabolic energy production; overwhelming psychological or emotional demands; increased energy requirements to perform activities of daily living; excessive social and/or role demands; states of discomfort; altered body chemistry (e.g. medications, drug withdrawal, chemotherapy).

Source: Voith, A., Frank, A., and Pegg, J. (1989). Nursing diagnosis : fatigue. In R. Carroll-Johnson (Eds.). Classification of Nursing Diagnosis : Proceedings of the Eighth Conference. p. 543. Philadelphia : J.B. Lippincott.

accepted for clinical testing as a nursing diagnosis by the North American Nursing Diagnosis Association (Voith, Frank and Pegg, 1989) - see figure 2.1. The 1990's have witnessed an increasing proliferation of research and Barbara Piper has emerged as a key worker.

2.4 Concept Clarification Of The Symptom Fatigue

2.4.1 Problems in definition

In the 1920's Muscio (1921) suggested that the term be abandoned altogether since what was called *fatigue* did not constitute a single entity, but a variety of unrelated phenomena. Others have challenged this view, believing that the difficulty in defining fatigue lay in a failure to appreciate its complexity (Bartley, 1965 ; Cameron, 1973). Despite numerous studies of fatigue and its causative factors, no interdisciplinary definition of fatigue has

emerged (Eidelman, 1980). Definitions of the nature of fatigue are numerous. Researchers in each discipline have their own definitions according to their experiences and perspectives.

Fatigue is a multifaceted, diverse concept. Despite concerted study, the complex phenomenon of fatigue is not well comprehended or clearly delineated. Possibly a contributing factor is the emergence of fatigue from a vocabulary of everyday conversational speech where a strict meaning has not been assigned to the term. Lay origins of the term may partially account for fatigue being divergently used when referring to a decrease in work , appraisal of how a person feels, and physiological changes. Such a broad spectrum of use suggests a difficulty in arriving at a practical and inclusive definition, especially since the term has roots in physiology, pathology and psychology. Each discipline places its own parameters on the concept and uses its special focus for interpretation. Physiologists often consider fatigue as an objective decrease in physical performance and failure to maintain force/power during sustained muscular contraction. Much empirical work has focused on subjective and objective signs that occur in relation to physical workload. Pathologists view it as a prime indicator of neuromuscular or metabolic disorders. Psychologists, on the other hand, consider it to be a condition affecting the whole organism, including decreased motivation as well as deterioration of mental and physical activities. When used with such different meanings and applied in a diversity of ways this rapidly results in a confusion of ideas.

Fatigue is considered by many writers to be a perception that arises from the complex interplay of somatic and psychological factors (Potempa, Lopez, Reid *et al.*, 1986). Fatigue is a subjective self-evaluation of sensations associated with discomfort, decrease in motor and mental skill plus increased task aversion (Grandjean, 1970). It may be conceptualised as a state of increased discomfort and decreased efficiency resulting from expenditure of energy reserves. People's energy reserves become unbalanced through physiological, psychological or pathophysiological stress (Hart and Freel, 1982). Cameron (1973) states that evidence suggests a broad conceptualisation of fatigue as "a generalised response to stress over a period of time, with effects which may be either acute or chronic, or both, confined to the subjective state of the individual or extending into measurable aspects of his performance" (p.640).

Although a broad view is evident in the literature of fatigue being conceptualised as a generalised response to stress, no direct correlation has been found between the degree of stress and amount of fatigue experienced. Lack of a relationship between stress and fatigue may result through individual variations in temperament such as coping styles, ability to perform a task, or mental or physical fitness, and environmental factors related

to comfort such as noise, light, temperature and humidity (Longmeire, 1981). Motivation is an influential factor. Donaldson (1975) states that the duration of the stress response rather than its intensity is responsible for the sensation of fatigue.

When comparing these definitions it becomes evident that they differ along two dimensions. Fatigue can be described as a subjective sense of weariness or tiredness resulting from exertion or stress. Or it can be considered a condition of impaired efficiency, resulting from prolonged mental and/or physical activity or from an attitude of boredom from monotonous work (Hart and Freel, 1982). It is defined by some as a process, and by others as the effect itself. Bartley and Chute (1947) following a thorough analysis of the concept of fatigue considered that it ought to be used to describe the subjective feelings of lassitude and disinclination toward activity, and offered the term *impairment* to identify the true reduction in physical capacity which resulted from accumulated oxygen debt in the muscle tissues. He employed the word *decrement* to indicate a deterioration in quality of performance for reasons other than sheer physical incapacity. These three aspects were viewed as holding complex relationships. Bartley (1976) concludes that it is more important, at this point, to use the term fatigue to label the experience syndrome, and defined fatigue as the "aversion to activity, a condition of existence expressed in bodily feelings, a self-felt assessment of inadequacy and the experience of futility, etc., with the desire to escape" (Bartley, 1965, p.7) and urges us to find other terms to label conditions and processes.

On the other hand, fatigue can be experienced by an individual without sense of futility or the desire to escape, for instance, the individual who experiences a sense of accomplishment with a job well done. In this situation the subjective feeling of fatigue is viewed positively, the implied sense of futility and the desire to escape are absent (Piper, 1986). Bartley's definition does not take into account the possible influences of circadian rhythm or the duration of the fatigue sensation, which may influence individual perception. Because of these inadequacies Piper coined a definition of fatigue thus : "a subjective feeling of tiredness that is influenced by circadian rhythm. It can vary in pleasantness, intensity, and duration. When acute, it serves a protective function ; when it becomes unusual, excessive, or constant (chronic), it no longer serves this function and may lead to aversion of activity with the desire to escape" (Piper, 1986. p.220). This definition reflects a nursing perspective and is based in clinical nursing experience.

The subjective view of fatigue is of particular concern to nurses caring for cancer patients. Nursing has viewed fatigue as a problem which interferes with recovery and maintenance of function. It has been defined as the perception of tiredness, lack of energy and inability to continue (Kellum, 1985). In tailoring a definition to the person

with cancer, Aistars (1987) outlines fatigue as a conditioned characterised by "subjective feelings of generalised weariness, weakness, exhaustion, and lack of energy resulting from prolonged stress that is directly or indirectly attributable to the disease process" (p.25). Fatigue involves more than a tired muscle, physiological processes, or decreases in work output, and any attempt to define this phenomenon is incomplete without the person's evaluation of his feelings. Fatigue is a person's total response to physiological, psychological, and situational factors.

In summary, fatigue has been conceptualised in the past in simple energistic terms or as a loss of energy or a decrement in physical performance. This has resulted chiefly because so much of the research concerning fatigue has been conducted in industry and physical education. Nursing cannot effectively adopt concepts conceived for another purpose. Attempts to further develop the concept would be beneficial. The role fatigue plays in health maintenance, illness, and rehabilitation is ambiguous. As long as the ambiguity exists, nursing interventions and nursing research related to fatigue will have little logic (Rhoten, 1982).

2.4.2 The fatigue continuum

In the literature tiredness and exhaustion are viewed as separate concepts from fatigue, or thought to differ in degrees of intensity. The commencement and cessation of fatigue are also undefined events. Grandjean (1970), a prominent worker in industrial fatigue and a noted psychologist and fatigue theorist, further delineates fatigue as one phase on the continuum of experiences people encounter as they move from a subjective state of feeling tired to a state of complete exhaustion. Tiredness, a part of normal, healthy living, is a state in which a person feels a generalised lessening of strength and energy. Such tiredness, it is considered, can easily be dispelled by sleep and rest, or by increasing nourishment and/or fluid intake. Exhaustion at the end of the fatigue continuum occurs when the expenditure of the body's reserves exceed its ability to replenish these reserves, forcing the body to stop functioning. The subjective feeling of general fatigue is described as a non-specific state indicative of a decreased level of vitality, which has the protective function of forcing the body to avoid further stress, thus allowing recovery to take place. Carpenito (1989-1990) similarly differentiates fatigue from tiredness.

Fatigue occurs in varied manifestations - from normal, acceptable tiredness to the state of exhaustion. Are there subtle nuances between a healthy tiredness and a gradual slowing down due to age and that tiredness associated with disease ? Morris (1982) notes that in health people feel well, are relaxed in manner, engage in recreation, and reject

pressures that could cause ill health. Others see them as healthy, adaptive, approachable, capable of rapid flexible thought, and vigorous enough for sustained activity. The term *acceptable fatigue* includes recognition of tiredness and steps taken to overcome it as soon as possible. People are perceived as healthily tired - their tiredness does not make them anxious. Fatigue is normal, and indeed essential, when the body is in need of rest for repair and restoration (Minden and Reich, 1983). The juncture where normal becomes abnormal fatigue is difficult to distinguish.

2.4.3 Feelings of fatigue

A variety of terms label the same condition, so fatigue has synonyms and partial synonyms like tiredness, lethargy and weariness (Bartley, 1976). It forms part of the experiential meaning of many terms. Fatigue is sometimes used synonymously with feelings of anxiety, uncertainty, depletion, nervousness and tension. These feelings may stem from physical incapacity, environmental deprivation or psychological failure. It is a matter of some urgency that we attempt to clarify terms such as malaise, lassitude, lethargy, weariness, fatigue and tiredness. Do such terms include a common denominator or is the sensation distinct enough ? A form of emotional experience appears to be an important aspect of the feeling of fatigue. Unfortunately interpretation is imprecise. It is unclear whether the feeling of fatigue refers to a primary or to a composite feeling-state and whether the peripheral or somatic manifestations of fatigue are essential aspects of the concept. As a consequence, whether it is possible to deal with the subjective and objective components of feelings of fatigue independently is unknown. Berrios (1990) asserts that it is possible to clarify the semantics by asking a number of questions:

- Do the terms outlined include a common denominator in either the primary sensation or in its attending somatic experiences ?

- Is the sensation that constitutes the feeling of fatigue distinctive enough to be qualitatively separated from mild pain or discomfort ? Fatigue historically has been considered a primary composite experience.

- Regardless of whether fatigue is a primary sensation, can it be recognised independently from its usual causal mechanisms ?

- Is an unexplained feeling of fatigue phenomenologically identical to the feeling experienced after exercise? Answers to such questions must be sought in empirical research.

- If the feeling of fatigue is considered a primary experience, then is it related to a common neurobiological structure or mechanism ?

The same author asserts that the feeling of fatigue has received much less attention in the literature than the general phenomenon of fatigue. He defines the feeling of fatigue as " a primary, *sui generis feeling,* which can be studied (and is experienced) independently of physical phenomena such as tiredness, and cognitive concomitants such as not wanting to continue or initiate a task" (p. 148). The first stage in identification of the semantic construct of the feeling of fatigue is to tease out its meaning systems. Four are apparent:

- Feeling of fatigue after work. In this situation the experience is explained by its precursor and is often associated with the realisation of not wishing to continue performing. This constitutes the typical, anchor meaning.

- Premature feelings of fatigue. Premature feelings of fatigue result when the experience is reached too quickly or when recovery takes too long.

- Unexplained feelings of fatigue. Unexplained feelings of fatigue cause alarm because they have no relevant antecedent. The experience may also be accompanied by a feeling of not wishing to begin any task. This meaning is common in relation to physical and psychiatric disease.

- Not wishing to embark on any activity. Feeling as though one does not wish to begin any activity may occur in the absence of a feeling of fatigue and probably is an independent phenomenon. Historically and clinically the two sensations have been lumped together.

These four meaning systems should generate different questions and must be clearly separated. They also may lead to different predictions with regard to correlations between the experience of the feeling of fatigue and objective measures of fatigue (Berrios, 1990). A conceptual confusion exists, indicating the need for phenomenological studies concerned with the feeling of fatigue.

Kinsman and Weiser (1976) proposed a model that commences with discrete symptoms, forms categories of symptoms and finally converges into a global feeling of undifferentiated fatigue, indicating that discrete symptoms may be organised into related but unique categories when examining fatigue in relation to work. They acknowledged that specific symptoms and symptom categories may change substantially between tasks.

Fatigue has thus become a word with vague, multiple and conflicting meanings. Bartley (1981) describes typical uses of the word fatigue and goes on to suggest that *fatigue* could be the term for the personal state, regardless of how it is detected, with *tiredness* and *weariness* the names for the person's own feelings. *Impairment* should be the term used to indicate a body part is not functioning normally.

It seems possible to make an important distinction between fatigue and weakness. Weakness involves muscular strength and function. A complaint of weakness implies a neuromuscular problem. Muncie (1941) differentiates tiredness, the result of effort, from weakness, the forestaller of effort.

Several physiological concepts are related to the fatigue phenomenon. These concepts include anorexia, cachexia, pain, dyspnoea, sleep, stress, and rest. To what extent each contributes to or is distinct from the other(s) in defining characteristics requires further study.

It would be helpful to reach mutual consent in nursing of the concept and the terms in this area. Differing conceptual frames of reference and countless definitions have compounded the vagueness of the concept and impeded comparison of research results.

2.5 The Origin And Mechanisms Of Fatigue

2.5.1 Pathophysiological explanations for fatigue

Our understanding of the pathophysiological mechanisms of fatigue are incomplete. Numerous competing hypotheses exist. Explanations are often speculative and preliminary. Formal investigations of fatigue have focused almost entirely on muscle fatigue, emphasising this as the primary basis for the fatigue experience. Mechanisms underlying the fatigue of human skeletal muscle have been discussed under the auspices of the Ciba Foundation (Porter and Whelan, 1981) and Edwards (1981) reviews the development of ideas concerned with fatigue in human muscle. McFarland (1971) asserts that fatigue cannot be considered solely a simple physiological condition resulting from sustained activity, nor solely in terms of biochemical changes in the muscles or nerves or by exhaustion of energy reserves. Consideration should be given to the role of psychological variables. Fatigue has been related to selected mood states including depression and anxiety. The anxiety/depression/fatigue relationship is complicated. The existence of either state may react with and intensify the other. These perspectives do not

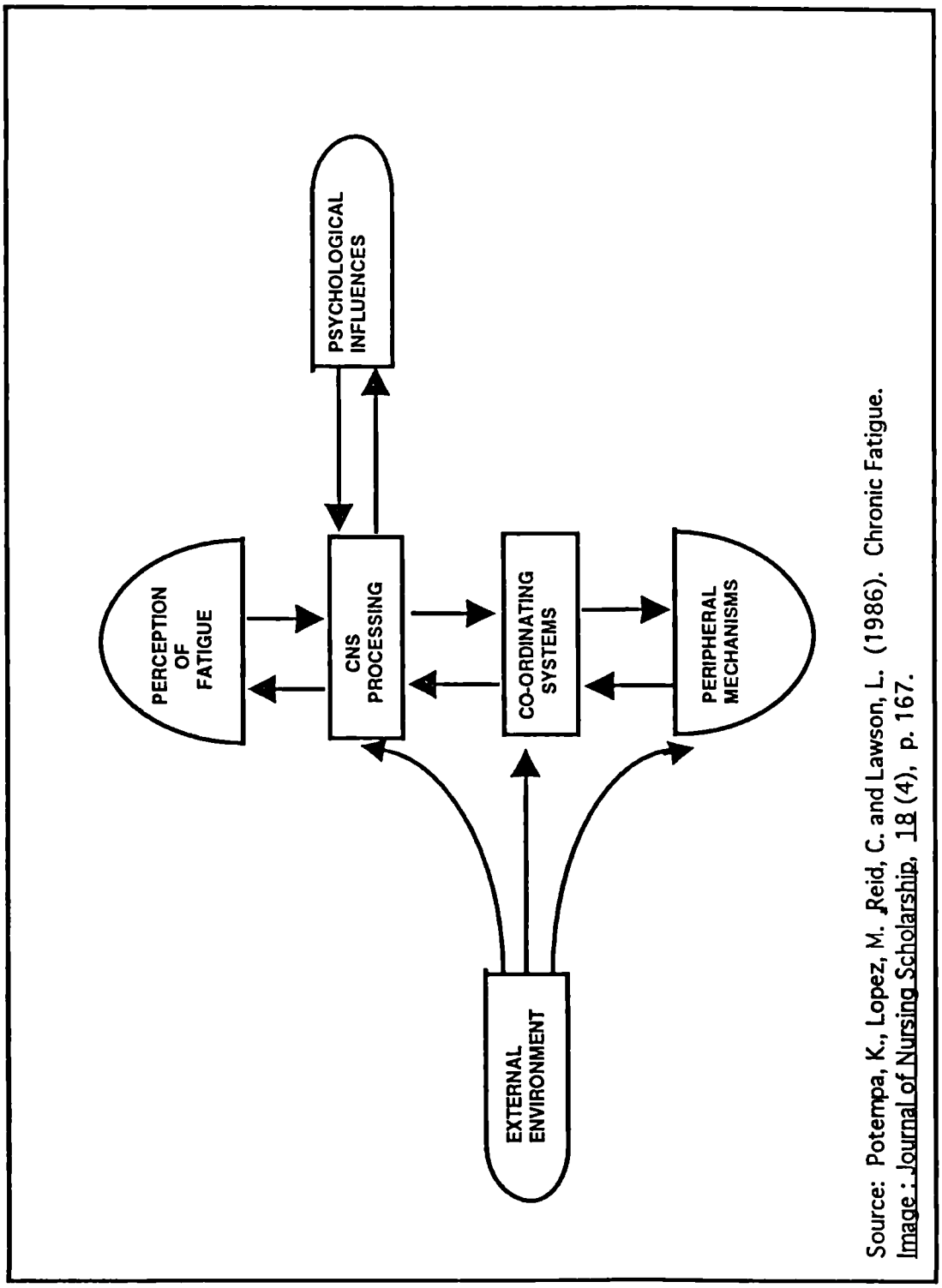
represent the full spectrum of the fatigue seen in clinical practice; yet there is much in the physiological and psychological literature that is relevant to the understanding of fatigue. Unfortunately, few attempts have been made to synthesise the aspects of this complicated construct in a clinically meaningful manner.

Fatigue may be related to physiological, psychological, and personality factors that may influence the manifestation, intensity, and duration of this phenemenon. Various theories and models have been proposed that explain how fatigue occurs and speculate on the influence and interaction of various factors. Potempa (1986) proposes a general model of fatigue which describes the integration of a variety of factors. It is a deductive model which utilises information from a variety of disciplines as well as the perspectives and clinical experiences of the authors. The multifactorial nature of fatigue can be clearly seen in the proposed model (figure 2.2) which depicts the organism as an open system that is affected by both internal and external events. This descriptive scheme is useful in that it is integrative and relates interacting variables. However, caution is required as more information is needed about the conditions that can modify these variables and their interactions before the occurrence and degree of fatigue can be predicted.

Eidelman (1980) proposes a physiological formula for fatigue, based on the concept of a reduction of the *latent capacity* of cells, tissues and organs whose states are constantly monitored by the brain. Reduced *latent capacity* is postulated as being the common thread in the different kinds of fatigue (physiological, pathological, psychogenic and acute and chronic).

It is postulated that fatigue is the mechanism within the brain which monitors a decrease in the *latent capacity* of tissues and organs. This is then translated as a graduated resistance to continued activity - reduction or cessation of capacity being a prerequisite for the initiation of regeneration. The *latent capacity* is determined by a number of factors:

- specific function
- reduction of the number of cells
- factors affecting cell metabolism
- rest and sleep
- psychogenic considerations.



Source: Potempa, K., Lopez, M. ,Reid, C. and Lawson, L. (1986). Chronic Fatigue. Image : Journal of Nursing Scholarship, 18 (4), p. 167.

Figure 2.2 A model of fatigue

The centrally monitored need for regeneration is suggested as being the sought-after common thread and the concept of fatigue is viewed as an expression of reduced *latent capacity*. It is proposed that fatigue is the mechanism whereby slowdown or cessation of function is initiated thus allowing regeneration. It is also the mechanism which prevents overuse of individual tissues or organs within the overall physiological framework of the body.

Pathophysiological mechanisms contributing to the phenomenon of fatigue may be grouped into four categories :

- accumulation of metabolites
- depletion of energy-yielding substances
- changes in regulation or transmission
- humoral factors.

Piper (1987) generated a framework that integrates these mechanisms and considers them as the most probable causes of fatigue in clinical populations. However, it is chiefly based upon mechanisms in healthy people. Accumulations of various metabolites have been associated with fatigue. Whether these products cause fatigue or merely parallel its occurrence remains unknown. In clinical populations the accumulation of lactate, hydrogen ions and the end products of cell destruction are potential factors. Changes in energy production and substrates can influence human performance and fatigue. These changes may result from abnormalities in energy expenditure, cancer cachexia, anorexia, infection, fever and imbalance in thyroid hormones. Depletion of muscle glycogen can occur with continuous muscular work. In cancer patients, prolonged anorexia, accelerated energy utilisation, and depletion of fat reserves can occur, which may result in an increased incidence in reported fatigue. Cholinergic and adrenergic drugs have also been implicated (Kaye, 1980). In addition serotonin plays an important role in the state of sleep. Accumulation of serotonin induces sleep while depletion of serotonin results in a marked loss of sleep. Fluid and electrolyte imbalances or changes in neurohormone levels can affect neurotransmission and muscle force resulting in fatigue. A chemical substance has been postulated as an explanation for fatigue, but has not been isolated or otherwise conclusively proven to exist (Eidelman, 1980).

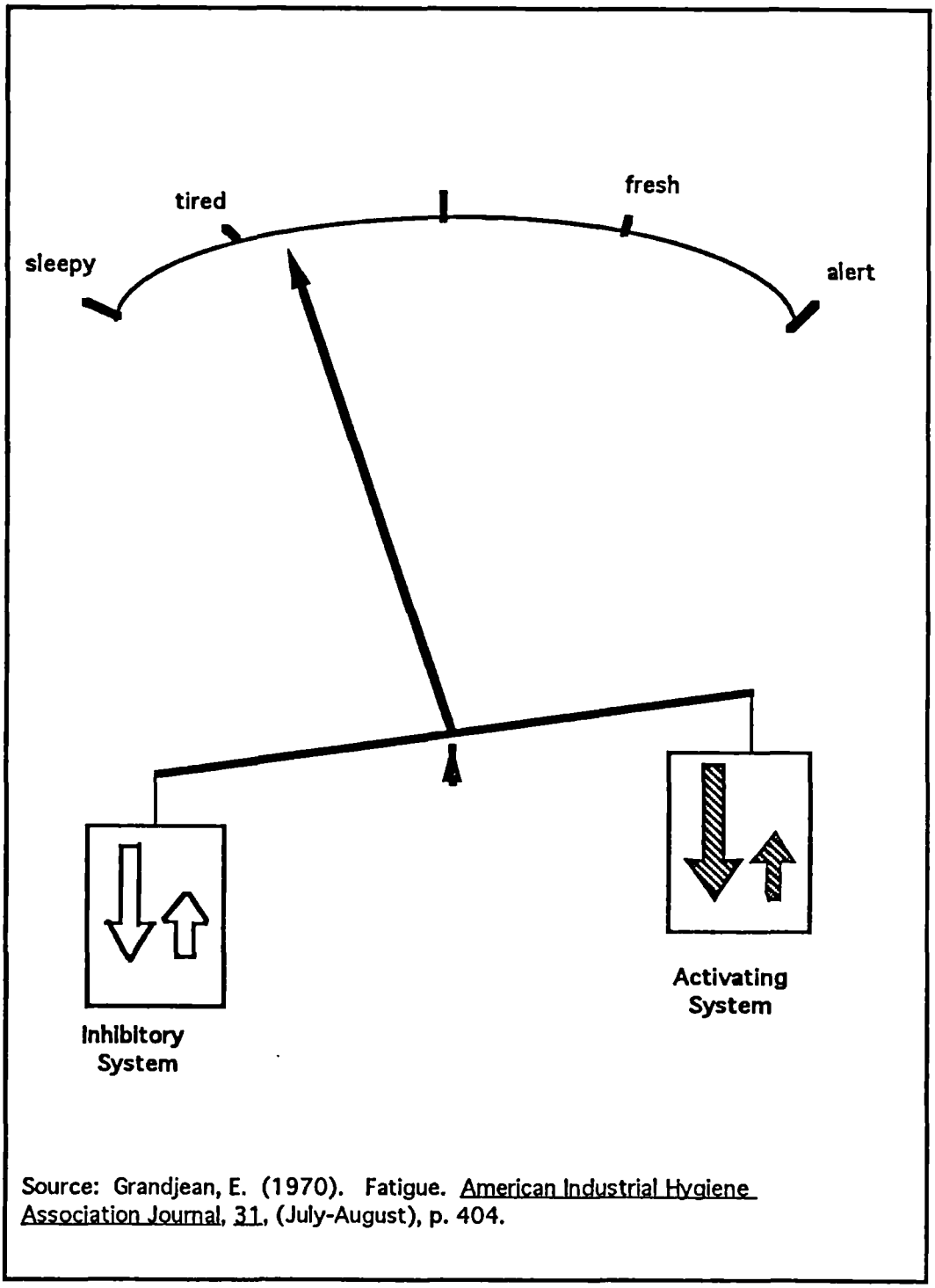
Generalised fatigue could be considered a central nervous system state controlled by antagonistic activity of the inhibitory and activating systems of the brain stem. These regulating or adaptive systems are susceptible to reactions to stimuli from the surrounding environment, to stimuli from the conscious part of the brain, and to humoral factors originating within the organism (Grandjean, 1970).

It is hypothesised that the most likely site for the central control of fatigue lies in the reticular formation of the midbrain and the medulla. These areas are related to consciousness and unconsciousness, arousal and depression, and to sleep and wakefulness. Grandjean (1970) proposed a neurophysiological model for alertness and fatigue. In this model (see figure 2.3) subjective feelings range from alert at one extreme to sleep on the other. Degrees of feelings can be explained by the antagonistic activities of the activating and inhibitory systems. The Reticular Activating System (RAS), located in the reticular formation of the midbrain, is responsible for maintaining wakefulness. A feedback system exists between the RAS and the cerebral cortex. Stimuli from the cortex trigger the ascending RAS, which in turn stimulates the cortex to maintain a state of arousal/wakefulness. Sensory organs responding to environmental stimuli stimulate the RAS through the afferent pathways.

Cortical inhibition can result either from an increased activity of the inhibitory system, which Grandjean calls *active* inhibitory function, or from lowered sensory input or decreased feedback, which he termed *passive* inhibitory function. It is hypothesised that a decrease in synaptic transmission occurs when the organism is exposed to continuous or monotonous noise or to boring, meaningless routine. This is believed to be a normal homeostatic mechanism that is designed to protect the organism from completely depleting its energy stores at the cellular level.

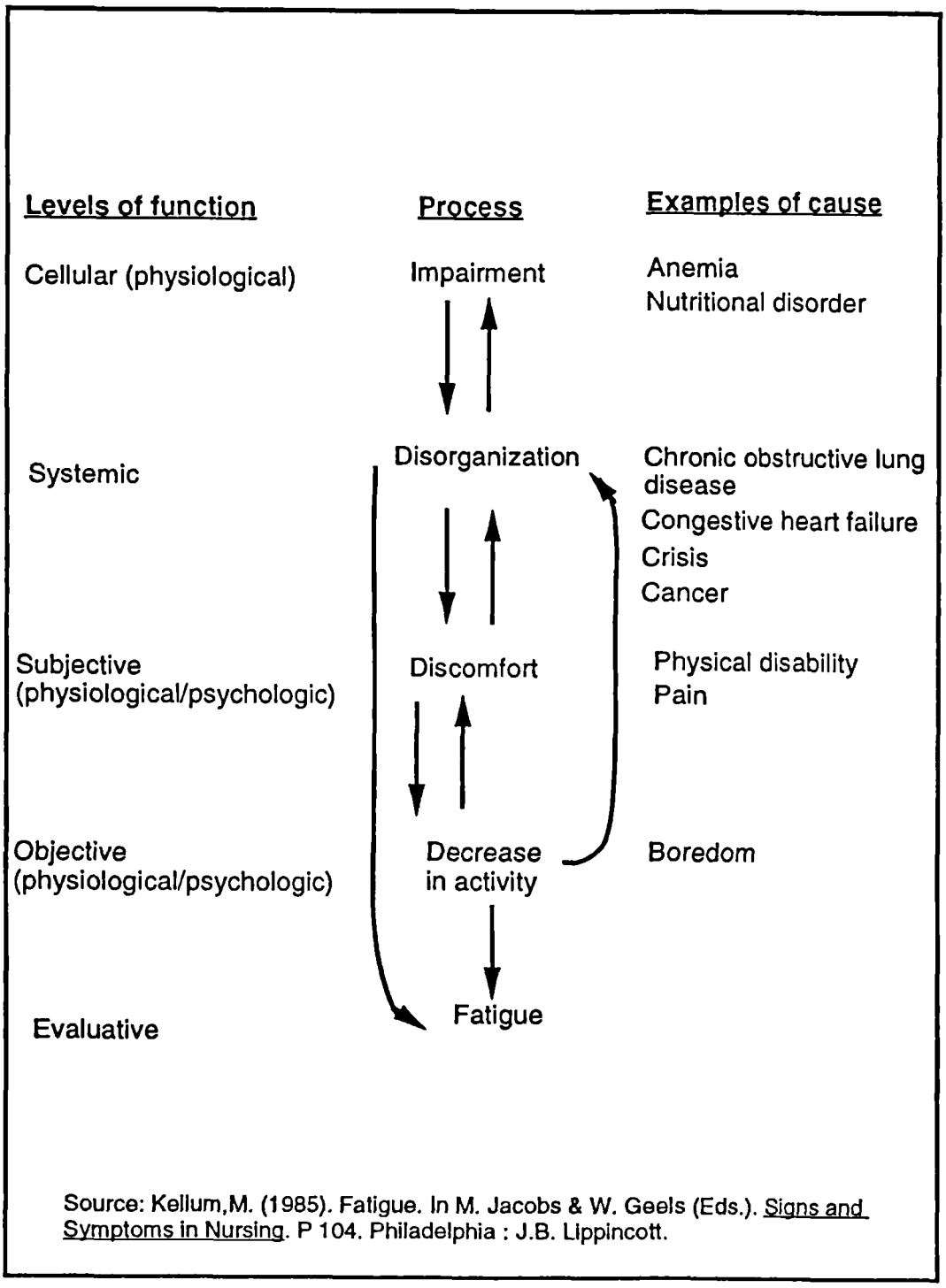
The psychologist Bartley has written extensively about fatigue and has developed an explanation of its pathophysiology that includes physiological and psychological components, their interactions and effects (Bartley, 1965). He describes a series of phenomena that lead to fatigue : impairment, disorganisation, discomfort and decrease in

Figure 2.3 Simplified scheme of the neurophysiological concept of fatigue



Source: Grandjean, E. (1970). Fatigue. American Industrial Hygiene Association Journal, 31, (July-August), p. 404.

Figure 2.4 The process of fatigue



Source: Kellum,M. (1985). Fatigue. In M. Jacobs & W. Geels (Eds.). Signs and Symptoms in Nursing. P 104. Philadelphia : J.B. Lippincott.

activity. Each occurs at a particular level of function : cellular, systemic, subjective, objective and evaluative. The initial disturbance can occur at any level, but eventually all levels become involved. Fatigue is the final, generalised response. The process as envisaged by Bartley has been represented visually by Kellum (see figure 2.4).

Impairment occurs at the cellular level. Impairment is the decreased ability of cells to function, which results from a depletion of energy stores and an accumulation of metabolic waste products. Repeated contractions of a skeletal muscle result in impairment : the fibres contract less effectively and recovery time is delayed. Impairment produces physiological and secondary psychological changes.

Disorganisation occurs at the systemic level of function and can result in fatigue. Body systems integrate the functions of cells, tissues and organs so they operate in unison. Disorganisation is the failure of a system to act in an integrated and effective manner. It is a crucial step in the process of fatigue.

Discomfort is the subjective experience of fatigue. For example, muscles will ache after repeated use. The sense of being unable to meet a demand or live up to a self-expectation also leads to feelings of discomfort. Sensory or cognitive discomfort can lead the person to cease performance before physiological limits are reached.

A decrease in activity is the objective result of this process. The person becomes less effective and work output decreases. The feeling of fatigue is the net response to the process. It is based on the evaluation of body feelings and sensations, the realisation that effectiveness has diminished and the urge to withdraw or discontinue activity. Fatigue can be a response that is normal or expected, protective or pathological. It can be viewed as an abnormal response, and the view taken will affect a person's reactions, self-expectations, and the expectations of the health care provider.

2.5.2 Fatigue as a protective mechanism

In medical and lay belief, fatigue is frequently regarded as something to be avoided entirely. Avoidance of fatigue may not, however, be wholly desirable if it is viewed in relation to the process of adaptation. The disagreeable sensations referred to as fatigue may be essential indicators that physiological equilibrium somewhere in the body is disrupted. It could indicate a mechanism whereby slowdown or cessation of function is initiated, allowing for regeneration and prevention of overuse of individual tissues or organs within the overall physiologic framework of the body (Eidelman, 1980). Fatigue

Table 2.1 Situational and developmental stressors associated with the development of fatigue

SITUATIONAL	DEVELOPMENTAL
Environmental e.g. noise, illumination, climate Drug related e.g. anti-depressants, beta blockers, Methyldopa Therapy related e.g. anaesthetics, radiotherapy and chemotherapy Physical exertion (prolonged or unusual) Non-physical exertion (boredom, monotonous mental work	Physical disease e.g. chronic pulmonary, renal and cardiac insufficiency, bacterial, fungal and viral infections, endocrine disorders, neuromuscular and neurological disorders, malignancy. Activity (too much and too little) Sleep and rest (inadequate or altered) Accumulation of recent stress and crisis Psychological (depression and anxiety) Maturation e.g. age, pregnancy Nutrition e.g. obesity, cachexia, anorexia

can therefore be considered a defence mechanism or a protective phenomenon, helping to maintain physiological equilibrium by stimulating a desire for work decrements or stress avoidance when the response to stress reaches a level of discomfort (Bartley, 1965; Bartley, 1976). Dixon, Dixon, and Hickey (1993) consider energy levels to hold a central status in terms of the conception of health, and speculate that changes in energy are an important precursor or early warning sign of ill health. Stressors potentially responsible in initiating fatigue are represented in table 2.1.

Norris (1982) names some basic physiological protective phenomena for nursing (e.g. nausea, chronic itching, immobility and tiredness) and evaluates them as concepts for nursing. All of the concepts studied appear to share enough elements to permit organisation under an umbrella named *basic physiological protective mechanisms.* The phenomena, identified in the pathophysiological framework as symptoms, are identified as protective (i.e. representing healthy coping behaviours) and refer to functional behavioural responses that attempt to remove threat to bodily organs or systems. Sleep disturbance, restlessness, and fatigue were identified as early protective responses. Possibly intervention at this point would promote rapid reinstatement of homeostasis.

The protective function of fatigue is "perceived by the organism as lack of energy or a tired feeling. It warns that energy production is not keeping pace with energy demands. Further, it warns that the organism needs to rest to protect against exhaustion that cannot be relieved by routine resting. Responding to fatigue by resting reduces energy consumption" (Norris, 1982, p.137). The feeling after responding to the protective warning is one of "relief, comfort, or reward to rest, coupled with pleasurable sensations" (Norris, 1982, p.392). Fatigue as a withdrawing activity is considered to have attributes

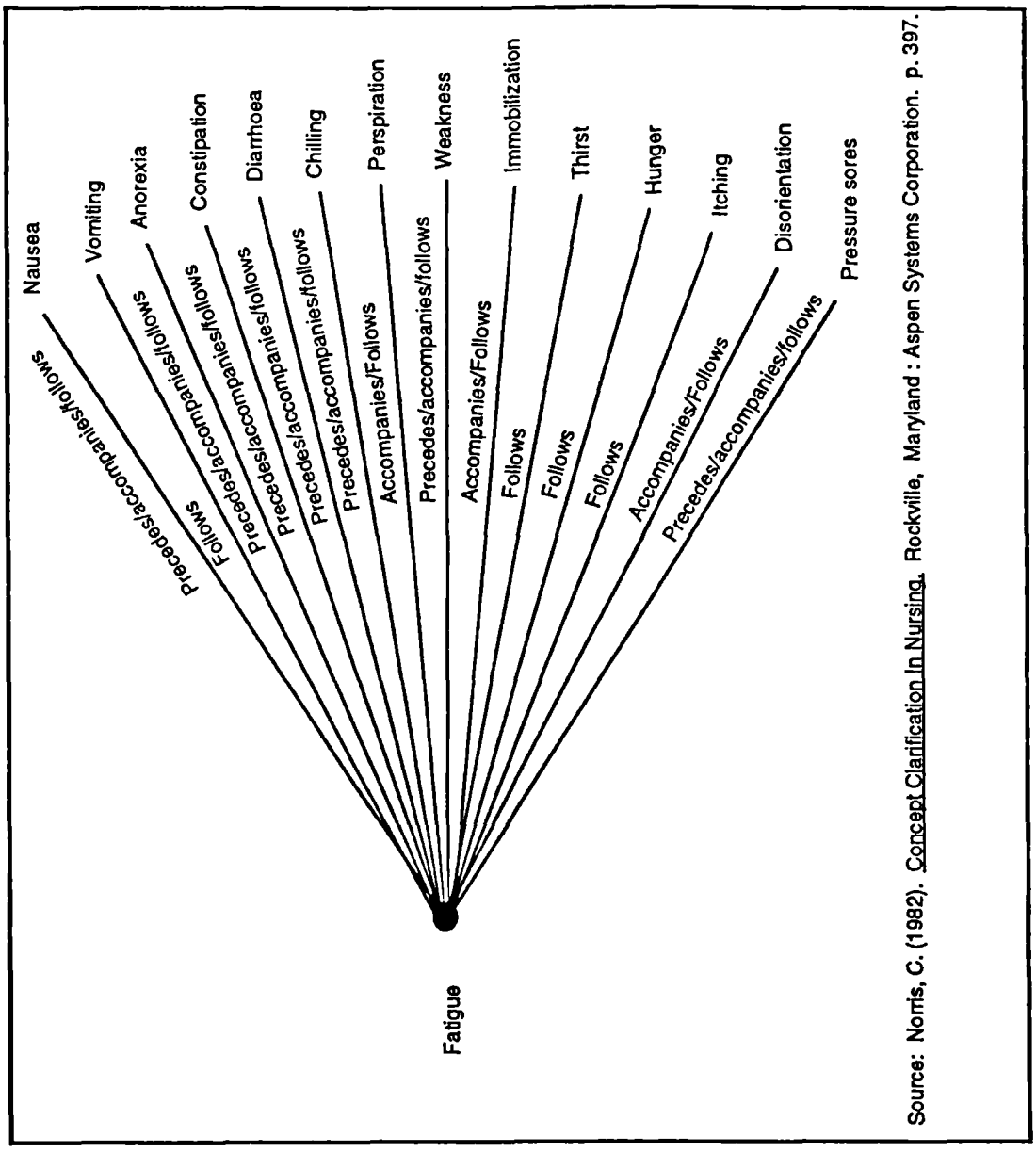
in common with immobilisation, nausea, anorexia, disorientation, chilling and shivering; that is it protects through the same general kind of protective response.

In addition to the search for commonality in the type of protection, relationships among phenomena are identified. Fatigue and restlessness are highlighted as they appear to be the most commonly occurring concomitants. It may be that fatigue has a common denominator relationship to the protective phenomena as illustrated in figure 2.5. If this is the case, that they are the most common physiological protective mechanisms, this would have implications for nursing priorities in health promotion.

In summary, fatigue-producing variables include physical, mental, emotional, environmental, physiological and pathological factors operating either separately or in combination. It is considered a complex protective mechanism mediated by stimuli from the environment, by stimuli from the conscious part of the brain, and by humoral factors within the organism. Aetiology of fatigue appears to be the result of the body's inability to maintain a state of equilibrium when faced with a stressor that taxes its homeostatic mechanisms (Bartley, 1965 ; Grandjean, 1968 ; Grandjean, 1969 ; Grandjean, 1970 ; Bartley, 1976). An understanding of the process of fatigue helps clarify the causative factors and their interactions. The actual mechanisms that produce fatigue even at the muscle level, are unknown. Cameron (1973), a pioneer in the investigation of fatigue, attempted to develop a theory of fatigue. He critically evaluated prior research efforts directed toward either measuring or defining the sensation and concluded that fatigue has its origin in the personal state of the individual. The author stressed that fatigue was mutidimensional and should be investigated with this in mind.

2.6 Classification Of Types Of Fatigue

To compound the definition issue, fatigue has been classified and categorised in a variety of ways. Many classification systems are found in the literature accompanied by the notion that we can speak of different kinds of fatigue. Several authors have categorised fatigue as mental, physical, physiological, nervous, pathological or emotional. In addition to these specific classifications of fatigue, causation has also been depicted in broader categories such as acute and chronic fatigue and into subjective (psychological/personalistic), objective (work output), and physiological domains. Subjective fatigue is a kind of experience, awareness, or feeling. Objective fatigue is exemplified in studies of work output and physiological fatigue is the kind involved



Source: Norris, C. (1982). Concept Clarification In Nursing. Rockville, Maryland : Aspen Systems Corporation. p. 397.

Figure 2.5 Fatigue in common denominator association with basic human physiological protective mechanisms

where selected body processes are found to change during performance of a task (Bartley, 1976).

Central and *peripheral* models have been suggested by physiologists (Merton, 1954; Gibson and Edwards, 1985). These muscle physiologists separate peripheral fatigue due to impairment of the peripheral nerve or connecting muscle, from central fatigue, manifested by deficits in the organisation, integration and motivation of muscle action. Central fatigue may be caused by lack of motivation and impaired transmission down the spinal cord. Peripheral fatigue may be due to impaired functioning of peripheral nerves, neuromuscular junction transmission or nerve fibre activation. Little is known about how these normal physiological mechanisms may be affected by abnormal processes such as disease states. Bass (1989) differentiates between fatigue symptoms of central and peripheral origin by dividing the components of the symptoms of fatigue into mental fatigue, problems with concentration and thinking clearly, and physical fatigue, a lack of strength in muscles and feeling weak.

Another useful delineation of fatigue is to categorise it into local-muscle, general-muscle and generalised fatigue. Local-muscle fatigue is a singular entity occurring after use of a local muscle group. This condition may be due to a malfunction in impulse transmission (Nachmanson, 1960) or due to a change in the muscle itself, such as depletion of its glycogen stores (Bergstrom and Hultman, 1967). In general-muscle fatigue, muscle exertion may be one of many variables, but its production is primarily due to failure of circulatory and metabolic maladaptations rather than to local-muscle failure. A much broader phenomenon appears operative with generalised fatigue. This state, resulting in a decrement in performance, does not necessarily involve failure of muscular contraction or exhaustion of circulation or metabolic supply. Grandjean (1968) suggests the most likely site of central control of this generalised fatigue state is the reticular formation of the midbrain and medulla, since this area of the brain relates to consciousness, arousal and depression, sleep and wakefulness. This hypothesis has been described previously.

The classification system most useful to nursing practice (Piper, 1989) characterises fatigue as acute or chronic depending on the duration (Bartley and Chute, 1947 ; Piper, 1986 ; Piper, 1988). The impact of rest upon the ability to recover differentiates acute from chronic fatigue. Acute fatigue quickly responds to rest or sleep while chronic fatigue is little changed by either. Chronic fatigue is more likely to be temporarily decreased by an increase in activity, change in activity, or diversion. The literature

Table 2.2 Acute and chronic fatigue model ; distinguishing characteristics

Characteristic	Acute Fatigue	Chronic Fatigue
Purpose/Function	Protective	Unknown, may no longer be protective May be nonfunctional
Population at Risk	Primarily healthy individuals	Primarily clinical populations
Etiology	Usually identifiable	May not be identifiable
	Usually involves a single mechanism or cause	Usually multiple and additive causes
	Often experienced in relation to some form of activity or exertion	Often experienced with no relation to activity or exertion
Perception	Normal, usual	Abnormal, unusual
	Expected/anticipated with respect to specific activities or forms of exertion	Excessive or disproportionate to past experience
	Primarily localized to a specific body part or system	Generalized, whole body-mind sensation
Time Dimension:		
Onset	Rapid	Insidious, gradual Cumulative Threshold model
Duration	Short; days or weeks	Long; persists over time More than 1 month
Pattern	Intermittent/sporadic	Constant/recurrent
Relief Dimension	Usually alleviated by a good night's sleep adequate rest, proper diet, exercise program, or stress management techniques	Not completely dispelled by these methods A combination of approaches may be needed
	Resolves quickly	Does not resolve quickly
Impact on Activities of Daily Living and Quality of Life	Minor, minimal	Major

Source: Piper, B. (1988). Fatigue in cancer patients : current perspectives on measurement and management. In Nursing Management of Common Problems. Monograph from 5th National Conference on Cancer Nursing. p. 26. New York : American Cancer Society.

suggests differences exist between the two states (Bartley and Chute, 1947 ; McFarland, 1971 ; Cameron, 1973 ; Riddle, 1982 ; Potempa, Lopez, Reid *et al.*, 1986) and these are summarised in table 2.2.

Acute fatigue is generally defined as normal or expected fatigue of short duration, appears intermittently, and serves a protective function. Chronic fatigue is considered excessive, constant, may be cumulative and last for more than a month. Such simplistic distinctions may misrepresent the true nature of the variations and may be artificial or indeed arbitrary. The two states could co-exist in the same individual, as in the case of pain. Until the differences in acute and chronic fatigue are established, what the patient says must be considered reliable and valid.

In attempting to analyse the symptom Kellum (1985) found it useful to reflect on the common aetiological factors that lead to fatigue, and formed a set of diagnostic categories into which they fall. The author outlines and gives examples of the four categories of fatigue: normal, pathophysiological, situational and psychological.

Normal fatigue is an expected response to any exertion, change in daily activities, added stress, or a decrease in the physiological reserve. For example, a hectic schedule, prolonged physical exertion or an inadequate amount of sleep are all apt to lead to normal fatigue. Normal fatigue resolves quickly and predictably with rest and a moderate change in lifestyle. The person's restorative ability is important in diagnosing this type of fatigue.

Fatigue can also be a symptom of disease or the result of a pathophysiological process. Acute illnesses can be preceded and followed by periods of fatigue. Chronic disease can result in continual impairment of physiological reserve, predisposing the patient to fatigue. Ordinarily, the person cannot be expected to overcome the problem simply by resting and adopting changes in lifestyle : the person's restorative ability is diminished.

Situational fatigue is a variant of normal fatigue. It occurs in unusual, fairly transient circumstances that produce periods of extreme stress, during which normal coping mechanisms are inadequate. Crises occur when a person is confronted with a problem he is unable to resolve by using the usual repertoire of actions and resources. If the crisis continues without successful resolution, tension and discomfort build. Tension and discomfort, if prolonged or severe lead to anxiety, a sense of helplessness, and finally disorganisation. Fatigue is the response to the increase in energy that a crisis requires, and to the disorganisation and anxiety that an unresolved crisis creates.

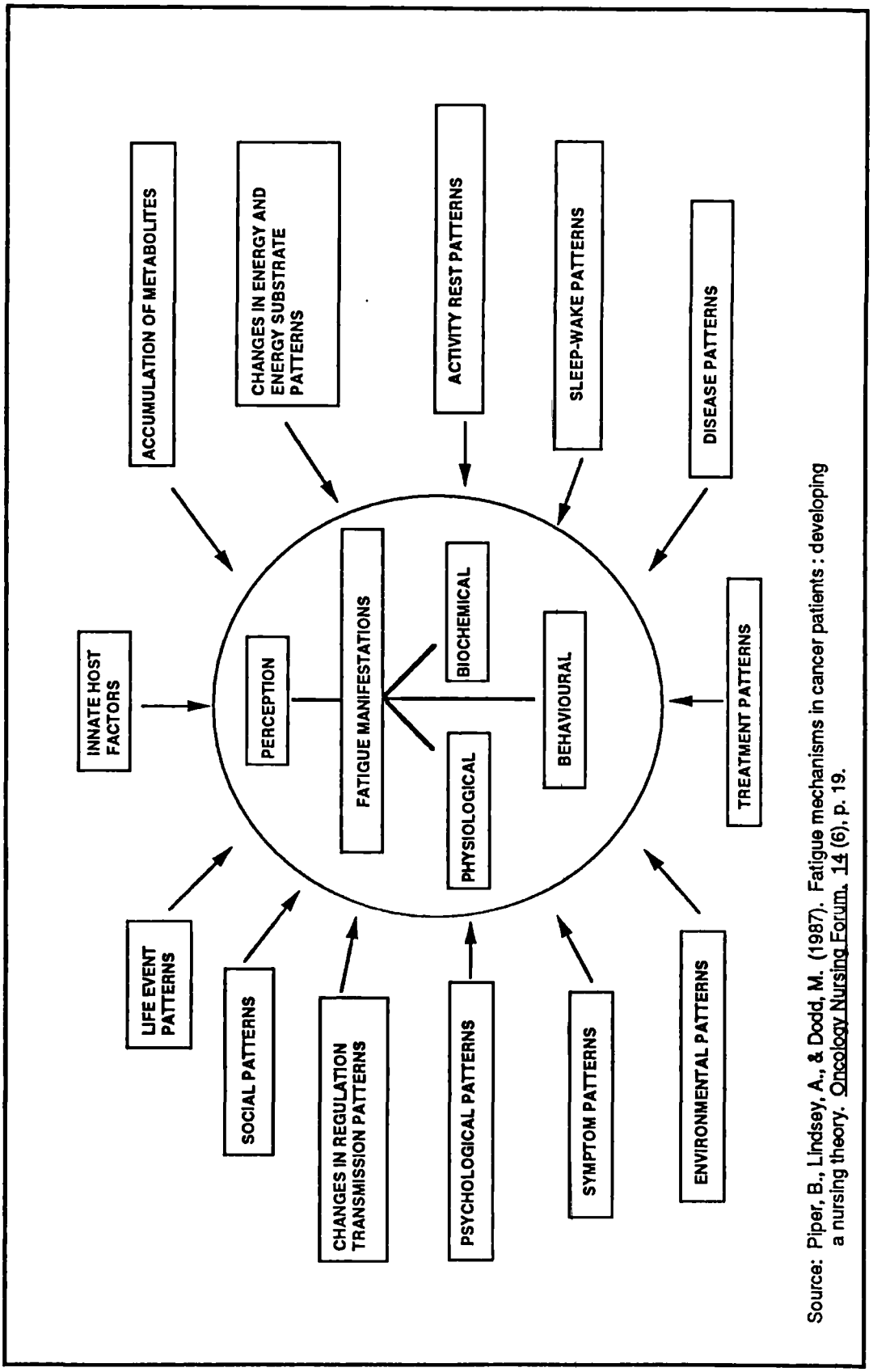
Finally, fatigue may be a symptom of significant psychological disorders, depression and anxiety being the most common causes. Fatigue is an evaluative response to the changes that take place in a person suffering from depression. These disorders are more chronic than situational fatigue. Currently when fatigue is discussed in the psychological and psychiatric literature, the focus is on the relationship between fatigue and depression. The essential features of a major depressive illness disorder are depressed mood or loss of interest in most activities. Energy levels are virtually always reduced, and the depressed individual often complains of fatigue even in the absence of physical exertion. The direction of the aetiological relationship between fatigue, depression and anxiety is unclear ; we do not know whether these disorders cause or are caused by fatigue. However, fatigue probably both contributes to and results from emotional disorders. All types of fatigue may occur in health and illness, and may at times overlap each other. It may be normal, a prodromal or concomitant to illness, chronic fatigue, or a mixture.

2.7 Populations At Risk

Some degree of fatigue is present in the community, it is found in nearly all the population, but only a small minority report severe fatigue. Some believe fatigue may acquire serious significance only in the older age groups. Indeed, fatigue may be the most universal symptom of old age (Klumpp, 1976). Fatigue in women has received distinct attention (Gendel, 1973 ; Riddle, 1982 ; Atkinson, 1985) particularly during the ante-natal and post-partum period (Milligan, 1988 ; Gardner, 1991 ; Pugh and Milligan, 1993 ; Milligan and Pugh, 1994).

Fatigue precedes, accompanies, or follows many diseases; it may be a universal precursor and sequel of a disease process. These include endocrine disorders, liver disease, nutritional disorders, neuromuscular defects, severe anaemia, cancer and cardiac diseases. People who have experienced an infection and undergone serious and extensive surgery and the critically ill can experience fatigue. In many chronic illnesses such as cancer and multiple sclerosis, fatigue is the most common, disruptive, and distressing symptom experienced because it interferes with self-care activities (Hart, 1978 ; Rhodes, Watson and Hanson, 1988). Piper (1989) proposed a multidimensional model designed to explain the complexity of fatigue associated with illness. Influential mechanisms in the fatigue experience are outlined in figure 2.6.

Individuals who are at higher risk for developing unusual, excessive, or prolonged fatigue include those who have undergone change or loss (single or multiple losses such



Source: Piper, B., Lindsey, A., & Dodd, M. (1987). Fatigue mechanisms in cancer patients : developing a nursing theory. Oncology Nursing Forum, 14 (6), p. 19.

Figure 2.6 Fatigue framework for the conceptualisation of fatigue in health and clinical populations

as family, job or money) and persons who have suffered prolonged anxiety. Family members who sustain the patient through a severe trauma or lengthy illness are vunerable to fatigue.

It is an important symptom because it affects a person's sense of well-being and ability to function. When a person experiences fatigue, he is unable to continue activities, may fear an illness, or may be very dissatisfied with his inability to perform or achieve a desired goal. It can have widespread effects, impeding the person in daily activities and detracting from the overall satisfaction with life.

2.8 Fatigue In Primary Care

A large proportion of the population experiences occasional fatigue and it has been confirmed as a common and perhaps universal complaint in both primary care (David, Pelosi, McDonald, Stephens, Ledger, Rathbone and Mann, 1990) and community studies (Chen, 1986 ; Cox, Blaxter, Buckle, Fenner, Golring, Huppert, Nickson, Roth, Stark, Wadsworth and Whichelow, 1987) both in Britain and the United States. A review of the literature on this subject, however, reveals a surprising lack of specific information, and it is a neglected topic of research. Most studies have focussed on the underlying cause of the symptom and have concluded that less than half of patients with fatigue have an underlying physical illness. Several papers have suggested that the majority of fatigued patients have psychological or emotional problems (Hargreaves, 1977 ; Sugarman and Berg, 1984 ; Manu, Matthews and Lane, 1988). A number of studies have now shown that the symptom of fatigue is strongly associated with anxiety and depressed mood and furthermore, psychiatric disturbance is a prominent feature of chronic fatigue syndrome.

It has aroused recent interest (Solberg, 1984 ; Sugarman and Berg, 1984 ; Smith and Scheinberg, 1985 ; Valdini, 1985 ; Kroenke, Wood, Mangelsdorff, Meier and Powell, 1988 ; Valdini, Steinhardt, Valicenti and Jaffe, 1988). Reports have been anecdotal (Allan, 1944 ; Jerret, 1981), or studies have been retrospective utilising chart review, or short term prospective designs (Morrison, 1980 ; Sugarman and Berg, 1984). The reports of Valdini, Steinhardt, Valicenti *et al.* (1988) and Kroenke, Wood, Mangelsdorff *et al.* (1988) are exceptions. To better understand the complaint of fatigue Valdini and his co-workers identified 115 fatigued adults and 139 who were not fatigued and followed them up with chart review, reassessment of fatigue scores and a telephone interview. The problem of fatigue was a dynamic one with many patients changing status from fatigued to non-fatigued over a one year period. The original fatigued subjects visited the clinic

more often during the follow-up year and received a greater number of new diagnoses than the non-fatigued.

The research studies confirm fatigue as a common problem in family practice, but provide conflicting estimates of the relative contributions of biomedical and psychosocial factors in the development of fatigue. Differing perspectives are evident, some studying fatigue as diagnosis (Morrison, 1980) and others who study it as a symptom (Valdini, Steinhardt, Valicenti *et al.*, 1988). Agreement is evident however in the view that laboratory investigations are of mimimal value in revealing cauastive agents. Patient populations are not comparable and often self-selected and non-random, practice sites vary and a lack of standard definitions or a standardised approach to investigation are often encountered in these studies (Valdini, 1985). The more recent studies, for example the study by Ridsdale (1993) have begun to address these limitations. A primary care perspective has much to contribute to research into the nature, causes and consequences of fatigue.

2.8.1 Chronic fatigue syndrome

An important difference that should be kept in mind is the difference between fatigue which is persistent in nature versus the chronic fatigue syndrome (CFS). CFS is characterised by the following:

- severe physical and mental fatigue induced by physical and mental effort
- myalgia, both at rest and on exertion
- an absence of abnormalities on conventional medical investigations
- duration of at least six months. (Wessely, Butler, Chalder and David, 1991, p.305)

The term itself has been introduced in an attempt to improve the comparability and reproducibility of clinical and epidemiological studies (Holmes, Kaplan, Gantz, Komaroff, Schonberger, Straus, Jones, Dubois, Cunningham-Rundles, Pahwa, Tosata, Zegans, Brown, Schooley, Brus and Purtilo, 1988), alternative terms include post viral fatigue syndrome and myalgic encephalomyelitis (ME).

Traditionally investigators have believed that CFS is a disease entity that may follow infection by one or more viruses, such as the Epstein Barr virus (Straus, Tosato, Armstrong, Lawley, Preble, Henle, Davey, Pearson, Epstein, Brus and Blaese, 1985), although support for this view is by no means widespread and interesting historical interpretations are available. The debate of organic versus functional causes is now being

gradually replaced by a multifactorial perspective which includes immunological, histopathological, psychoneuroimmunological, cognitive and behavioural factors (David, Wessely and Pelosi, 1988). This is best demonstrated in the model postulated by Wessely and his team at the Institute of Psychiatry, London (Wessely, Butler, Chalder *et al.*, 1991), who have encountered success when utilising cognitive behavioural techniques in the management of this syndrome (Wessely, David, Butler and Chalder, 1989).

2.9 Empirical Research Concerned With Fatigue In Illness

Interest in the sensation of fatigue has expanded to include not only evaluating healthy people experiencing acute fatigue associated with work-related situations and exercise but also to studying sick individuals experiencing chronic fatigue associated with their illness. Understanding the fatigue experience, whether acute or chronic, is significant to nursing because it is one of the most common problems associated with all health-related disorders. A series of studies attempted to measure the presence and experience of fatigue in different populations : surgery (Rose and King, 1978 ; Christensen, Bendix and Kehlet, 1982 ; Zeiderman, Welchew and Clark, 1990 ; Reid, 1992), renal disease (Cardenas and Kutner, 1982), rheumatoid arthritis (Tack, 1990a ; Tack, 1990b) multiple sclerosis (Freal, Kraft and Coryell, 1984 ; Krupp, Alvarez, LaRocca and Scheinberg, 1988), systemic lupus erythematosus (Knippen, 1988) chronic pulmonary conditions (Kinsman, Luparello, O'Banion and Spector, 1973 ; Kinsman, O'Banion, Resnikoff, Luparello and Spector, 1973 ; Janson-Bjerklie, Carrieri and Hudes, 1986 ; Gift, 1991) and congestive heart failure (Schaefer, 1990). Such reports document the significance of this symptom and the effect on a patient's quality of life.

Incidence data related to fatigue are difficult to accumulate. The incidence is frequently underestimated, since it is not considered unusual by health care providers, and patients may not be asked about its presence. Patients may hesitate to report anything so common and may not volunteer that they are experiencing fatigue unless it becomes prominent or impedes important aspects of their lives. Anticipation of fatigue by providers of care and by patients tends to reduce its importance and therefore its reported incidence (Morris, 1982).

Some research pertinent to fatigue in illness has been directed toward development of instruments to measure the phenomenon. This will be discussed in Chapter 3. The studies in table 2.3 are examples of nursing research whose discrete focus was to measure the subjective description of fatigue in clinical populations. It is clear from the research literature that fatigue is a serious symptom that has been observed in many clinical

Table 2.3 Summary of nursing research concerned with fatigue associated with illness

Study Ref.	Sample & Aims	Study Design	Instruments	Main Findings
Schaefer & Potylyctic (1993) Fatigue associated with congestive heart failure : use of Levine's conservation model	Congestive Heart Failure $n = 38$ 1. To describe the fatigue experience in patients with congestive heart failure related to myocardial injury and valvular dysfunction. 2. Determine the relationship between selected objective parameters and severity of fatigue in the patient with congestive heart failure related to myocardial injury or valvular dysfunction.	Descriptive/correlational Retrospective	A Fatigue Interview Schedule derived from the Piper Fatigue Scale and including items concerned with; Severity of fatigue (visual analogue scale, graphic rating scale and numerical rating scale) Mood - items from Profile of Mood States Activity level Social Integrity A chart review of physiological data	71% of patients were fatigued on admission, 24% were fatigued when interviewed, 55% said it occurred once in a while. Age was positively related to severity of fatigue, $r = .39$, $p < .01$. No relationship was found between severity of fatigue in general and other physiological measures. Moderate to high significant correlations were found between 3 tools used to rate fatigue. Patients described fatigue as being tired and exhausted, and containing both physical and emotional components. Reasons for fatigue fell into 4 categories; stress, physical activity, disease and cigarettes.
Cohen & Hardin (1989) Fatigue in patients with a catastrophic illness	Botulism $n = 25$ A control group n not specified To explore the length of time after botulism that fatigue feelings persist, and the times of day at which these patients experienced the greatest fatigue.	Descriptive/correlational Retrospective (before hospitalisation) and prospective (during hospitalisation and during home visits over 3 years)	Pearson Byars Fatigue Feeling Checklist Fatigue Symptom Checklist	Total fatigue score before botulism was 21.5 (range 10 - 60), and in hospital, 48.9. Three years after, the total fatigue score remained higher than before botulism at 29.7. RMANOVA showed total fatigue score significantly higher during hospitalisation and at each of the data collection points, up to 3 years after the onset of botulism ($F(7, 140) = 31.96$; $p < .0001$). The normal fatigue pattern was that persons were most alert one hour after awakening, and became steadily more fatigued throughout the day, the same as in a control group. The trajectory was disturbed during hospitalisation, subjects were highly fatigued throughout the day.

Table 2.3 (cont'd) Summary of nursing research concerned with fatigue associated with illness

Study Ref.	Sample & Aims	Study Design	Instruments	Main Findings
Hart (1978) Fatigue in the patient with multiple sclerosis	Multiple Sclerosis n = 335 (split into 4 groups dependent on mobility status) Healthy controls n = 30 To identify : 1. If there is any difference in the level of fatigue feelings experienced throughout the day by the two groups. 2. If there is any difference in the type of symptoms experienced in the two groups. 3. If the patients with multiple sclerosis perceive different activities than healthy persons which (a) increase feelings of fatigue or (b) decrease them.	Comparative Retrospective	A postal questionnaire incorporating; McAlpine and Compston Self Rating System of Level of Mobility Pearson Byars Fatigue Feeling Checklist Modified Fatigue Symptom Checklist Information on activities to prevent or recover from fatigue , activities that precipitate fatigue.	Patients with MS, regardless of mobility level, experienced more severe fatigue throughout the day than did healthy subjects. Less mobile group experienced more severe feelings of fatigue than did healthy subjects. Disease symptoms were accentuated and there were greater indicators of emotional stress in the patient group rather than the healthy group when fatigued. No significant differences were found in the frequency of symptom categories of the checklist between subject groups. In general MS and healthy subjects did not differ in the type of activities that made them tired, the method most frequently used was napping.
Belza, Henke, Yelin, Epstein & Gilliss (1993) Correlates of fatigue in older adults with rheumatoid arthritis	Rheumatoid Arthritis n = 133 1. To describe the prevalence of fatigue in patients with rheumatoid arthritis. 2. To examine the relationship between fatigue and the use of health care services in patients with rheumatoid arthritis. 3. To identify the demographic, disease-related, and psychosocial correlates of fatigue in rheumatoid arthritis.	Descriptive/correlational Retrospective (previous week) panel design	Annual telephone interview and mailed questionnaire; Multidimensional Assessment of Fatigue - severity, distress, timing, degree of interference in activities of daily living Geriatric Depression Scale-short form Health Assessment Questionnaire Physical Exercise and Activity Index Sleep Survey Social Support Scale Arthritis Helplessness Index	On average, a high degree of fatigue was reported everyday, remained constant throughout the course of the week, and most often affected walking and household chores. A regression model with fatigue as the dependent variable revealed that 61% of the variance was accounted for by the combination of specific and disease related variables (cumulative R^2 .61 [F (12, 114) = 15.07, p<.0001]). A significant amount of the variance was explained by pain rating, functional status, sleep quality, female gender, comorbid conditions, and duration of disease.

Table 2.3 (cont'd) Summary of nursing research concerned with fatigue associated with illness

Study Ref.	Sample & Aims	Study Design	Instruments	Main Findings
Srivastava (1989) Fatigue in end-stage renal disease patients	End-stage renal disease $n = 27$ To identify the characteristics of the fatigue experienced by end-stage renal disease patients (specifically, fatigue level and symptoms)	Descriptive/correlational Cross-sectional	Karnofsky Performance Index Spitzer Quality of Life Scale (SQL) Fatigue Symptom Checklist (FSC) Level of fatigue - Clinical Aggregate Score, Graded Linear Scale, Pearson Byars Fatigue Feeling Checklist Beck Depression Inventory	Significant relationships were noted between the SQL and the scales estimating level of fatigue. All three measures of the level of fatigue revealed similar results, correlations were 0.87 or higher. Nine of the top 12 symptoms on the FSC were also experienced in Haylock and Hart's study of cancer patients, although the rankings differed, suggesting "being tired" appears not to be the same for everyone.
Rhoten (1982) Fatigue and the postsurgical patient	Abdominal Surgery $n = 5$ To clarify the concept of fatigue, and identify the manifestations of fatigue and the characteristics of those at high risk for fatigue in the postsurgical patient.	Descriptive Prospective (24, 48 & 72 hours post op)	Rhoten Observational Checklist (ROC, completed by 2 nurses simultaneously at three 15 minute periods at designated times) After each observation; Rhoten Fatigue Scale (RFS) Semi structured interview schedule	Extent of surgery, length of anaesthesia, amount of pain medication, number of abnormal lab values seemed significant. Categories of the ROC that showed major differences between most fatigued and least fatigued patients were general appearance, eyes, facial expression, speech, movement and attitude. The rankings of the levels of fatigue made by the two observers based on their observations and interviews correlated with subjective rankings made by patients on the RFS.
Crosby (1991) Factors which contribute to fatigue associated with rheumatoid arthritis	Rheumatoid Arthritis Phase 1 $n = 100$ Phase 2 $n = 15, n=12$(controls) The questions guiding the research were: 1. What are the factors which rheumatoid arthritis patients believe contribute to their fatigue 2. What are the relationships between the factors which contribute to fatigue and how are those factors related to the sensation of fatigue	Cross-sectional Phase 1 exploratory Phase 2 comparative	Modified McGill Pain Inventory EEG Sleep Studies Walking Time And Grip Strength Level of Fatigue (VAS)	Phase 1 elicited most frequently identified factors contributing to fatigue; disease activity, disturbed sleep, and increased physical effort. In phase 2 those subjects experiencing a disease flare had significantly ($p<.01$) more joint pain, significantly ($p<.05$) more fragmented sleep, and significantly reduced functional capacity as measured through walking time ($p<.05$) and grip strength ($p<.05$) when compared to the non-flare and control group. Fatigue levels of the subjects in the flare group were positively correlated with the variables under study.

contexts. Correlates of fatigue have included depression, emotional stress, anxiety, anger, age and low physical fitness.

Research is descriptive in nature, characterised by lack of control groups, inadequate description of instrumentation with insufficient reliability and validity in the sample under study and infrequent attempts to provide operational definitions as to what is understood by the term fatigue. Major limitations also include the lack of consistency in the selection of fatigue measures, failure to consider the physiological dimension of fatigue and absence of a nursing framework for the continued development of nursing knowledge. Recently Schaefer and Potylycki (1993) reported a qualitative assessment of the experience of fatigue. Inherent in the study was the attempt to test whether the Levine Conservation Model (Levine, 1991) provided a clinically valid model to study fatigue.

The applicability of any findings to other patients with chronic illness where fatigue may be attributed to differing mechanisms is at present hampered, especially as aspects of fatigue unique or similar to each are only revealed if instruments and methods are comparable. Nonetheless some aspects are likely to be applicable and various types of patients, illnesses and phases of illness should be measured and compared. Available data suggest that there are more similarities than differences in how the symptom complex manifests across conditions. Fatigue patterns need to be documented across replicated studies to generate practice theory.

Although the mechanisms that lead to fatigue in a variety of conditions are not completely understood, several variables acting singly or in combination may contribute to fatigue. Until the physiological basis has been discovered, it would seem prudent to identify other factors which may contribute to the sensation of fatigue in various populations. Studies should identify the intensity, duration, pattern and trajectory of fatigue and associated symptoms, examine relationships between fatigue and demographic, disease related and psychosocial correlates of fatigue. The value of such research would ultimately lie in the identification of starting points for designing interventions aimed at the prevention and amelioration of fatigue. Studies to determine the efficacy of nursing interventions for fatigue in its various clinical contexts are urgently needed.

CHAPTER 3

MEASUREMENT OF FATIGUE

3.1 Introduction

The purpose of this chapter of the review is to critically evaluate self-report measures of fatigue. The measurement of fatigue is of value to nurses in a variety of different settings. The chapter will begin with a brief overview of historical trends in the measurement of fatigue. Discussion of issues relevant to the use of self-report scales in its measurement will follow. A description and critique of the methods available for assessing the dimensions of the fatigue experience will be presented then directions for further development summarised.

3.2 History

The resistance of the problem of measuring fatigue is easier to understand if the logical weaknesses inherent in much of the research are made explicit. The historical background of research into fatigue has been examined by Cameron (1973) who charts the changes in emphasis over the last fifty years.

The impossibility of measuring objectively a personal experience such as fatigue was first pointed out by MacDougall (1899) who made the distinction between subjective and objective fatigue and stated that measuring the latter gave little information on the former. Despite this, an Industrial Fatigue Research Board was formed to produce a definitive test. Its report was couched in strong terms: "the term *fatigue* be absolutely banished from scientific discussion, and consequently that attempts to obtain a fatigue *test* be abandoned" (Muscio, 1921,p.45). A fatigue laboratory existed at Harvard until the second world war. However, its director, Forbes, reported failure to solve the problem (Forbes, 1943) and reiterated the previous sentiments of Muscio. Today, fatigue remains as difficult to measure as it was in 1921.

An historical review reveals a change in emphasis. Originally there was exclusive concern with quantifiable measures of variation in productive output. A series of studies attempted to measure changes in performance (in tasks that included mental as well as

physical effort) and to define the conditions under which performance was adversely affected. Electrophysiologically it is possible to measure fatiguability as an objective inability to sustain power, but this is not necessarily related to the subjective sensation of fatigue. There is a general correlation between subjective feelings of fatigue and physical workload, but this is not always confirmed by empirical work. It is now recognised that fatigue is essentially a personal experience which must be understood in terms of individual reaction to stress extending over a period of time (Cameron, 1973). Bartley (1976) suggests that we should consider the notion that fatigue is a condition that only the individual can identify in himself, since it is an experience. Currently it is acknowledged the best way to assess fatigue in clinical populations is to determine the person's own perception of the fatigue experience. Because fatigue is primarily a subjective experience, self-report is the most common approach used to measure it.

3.3 Theoretical Models

The method of measurement adopted by a particular researcher depends on the explicit or implicit definition from which he has worked. Results of fatigue studies are notoriously difficult to interpret and to apply in any practical context. One reason is the lack of an adequate definition of fatigue. There is concern about the absence of effort to establish exactly what the term fatigue means when it is used in different settings (Barofsky and Legro, 1991). The absence of any coherent theoretical framework has further compounded the difficulty. To measure fatigue it is necessary to first arrive at a definition of the concept and determine which aspects to measure (Varricchio, 1985). It is important to make explicit any theoretical model used to guide the understanding of fatigue, as decisions about choice of instrument should be based on the author's conceptualisation of fatigue.

3.4 Multiple Contexts Of Fatigue Measurement

The measurement of this phenomenon does not exist independent of time, place or a person's cognition. Language, habits and cultural conventions enrich the vocabulary associated with this concept. There is likely to be a temporal pattern variation between individuals, hence time of day may be related to fatigue ratings. The conditions under which the self-reports of fatigue are made should be as similar as possible between comparison groups: for example, rating at the same time of day, in the same place and in the presence of the same people.

Historically many of the fatigue tools were developed for a healthy workforce. It should be acknowledged that the assessment of fatigue should evolve to reflect the nature of the phenomenon in acutely and chronically sick individuals. For example, assessment of fatigue due to cancer will require some reorientation dictated by the nature of the disease, the psychological context of having cancer, types of fatigue in cancer and the dynamic and progressive nature of both the disease and its treatment. It is desirable that an instrument to estimate perceived fatigue should be easy to administer, possible to complete within a short period of time without adding to the fatigue already present and easy to score. It should also be useful in assessing changes in fatigue over time or comparing perceptions of fatigue across patient populations.

3.5 Domain Issues

Fatigue can be viewed as a single phenomenon or discrete variable, but it is probably more realistic to view it as a continuous dimension, experienced as a subjective internal state. The experience of fatigue is acknowledged as complex and includes several subjective dimensions or aspects such as temporal, trend, severity/intensity, affective, evaluative and sensory which have been identified in the literature. Initial work on defining such dimensions has been achieved by Piper, Lindsey, Dodd, Ferketich, Paul and Weller (1989). More work needs to be done. However, at this point in time there appear to be at least four distinct subjective dimensions that can be assessed in all fatigue patient populations. Subjective indicators are the key to the understanding of how fatigue may vary in healthy and ill populations. The subjective dimension has been measured primarily as the unidimensional feeling of tiredness (Pearson and Byars, 1956 ; Pearson, 1957 ; Heuting and Sarphati, 1966 ; McNair, Lorr and Droppleman, 1971 ; McCorkle and Young, 1978 ; Rhoten, 1982). Only recently has fatigue, like pain, been conceptualised and measured as a multidimensional construct using the statistical procedures of factor and key cluster analysis (Kinsman and Weiser, 1976 ; Yoshitake, 1978).

Various subdimensions have been identified. The sensory component, for example, includes the physical, emotional and mental symptoms of fatigue, while the affective (or reactive) component involves a patient's emotional reaction to fatigue and fears about what it may signal. Failure to incorporate aspects other than the severity dimension may lead to a loss of much clinically important information; for example, where the sensation may not be any more or less intense but the person is coping better. The targets of assessment should focus on the knowledge needed to plan successful management strategies such as intensity/severity, characteristics denoted by various descriptors, temporal pattern, fatigue strategies and the impact of fatigue on the patient and family.

Unfortunately, many of the instruments that measure subjective fatigue are limited by their failure to include the dimensions outlined or by poor reliability and validity ratings. This is an important area for tool development.

Measurement of the subjective nature of fatigue is primarily based on self-estimation of the state of fatigue. The objective manifestations of fatigue, the physiological, biochemical and behavioural components, although less well investigated by nurse researchers, should also be recognised.

3.6 Scaling Techniques For Subjective Feelings

Measurement issues surrounding the quantification of subjective states, such as fatigue, have received increasing attention in nursing in recent years (Wills and Moore, 1994). There are a variety of solutions to adequate measurement. Two general methodologies, psychophysical techniques and rating scales, have been relied upon when estimating subjective feelings. Psychophysical techniques are used to produce ratio scales for variables which involve judgements of the intensity or strength of perceived stimuli. Psychophysics involves the "description of the relationship between perceived change in a physical stimulus, the psychological dimension, and change in the objective intensity or quality of the stimulus measured in physical units, the physical dimension" (Kinsman and Weiser, 1976, p.340). Psychophysical techniques are of limited utility, since they cannot be applied readily to the measurement of the individual's perception of fatigue over time. For the most part, they have been applied to the measurement of the individual's perception of fatigue to an external stimulus, rather than to the measurement and perception of fatigue in relation to an internal stimulus, such as a disease process. Although more precise in describing relationships between stimulus levels and perceptions, subjective fatigue cannot necessarily be related to the external physical stimulus. There is no accurate way of identifying the intensity of the physical stimulus when in fact the precise origins of the physiological cues are not well understood.

Rating scales have enjoyed a wider application, largely because of the ease with which they may be used. These techniques may be grouped into non-dimensional single point measures, unidimensional rating scale techniques of undifferentiated fatigue and tiredness and multidimensional rating scales. Interval scales can be constructed to measure subjective qualities, but require the use of lengthy psychometric techniques. In the measurement of subjective qualities during work performance, interval scaling is best exemplified by the study of Pearson (1957). The inherent shortcomings of ordinal scales can be largely overcome in most applications. The intervals between ordinal scale points

often can be made to appear equidistant by careful selection of the verbal descriptions accompanying each scale point, physically representing the verbal descriptions at equal intervals, and by indicating equal intervals in the numbering of the scale points. Furthermore a zero point can be provided by anchoring the first category with "not present" indicating complete absence of the subjective quality. Such ordinal scales have been treated statistically as if they were genuine equal-interval scales, but the ratio scales have a true zero point representing the absence of the attribute measured while also providing magnitude measurement by equal intervals in the units of measurement. Psychophysical techniques are used to obtain ratio scales for subjective qualities.

More recently a third general methodology involving multivariate statistical procedures has been used to identify a variety of categories or dimensions of symptomatology, particularly in relation to work performance and asthma (Kinsman, Luparello, O'Banion *et al.*, 1973 ; Kinsman, O'Banion, Resnikoff *et al.*, 1973). The approach encompasses determination of the categories of subjective symptoms and how they are interrelated. Multidimensional analysis, such as factor analysis or key cluster analysis, provides means to identify sets of symptoms that group together to form such symptom categories, hence the essential complexity of the range of subjective qualities is not ignored.

3.7 Measurement Approaches In Clinical Populations

3.7.1 Assessing fatigue intensity/severity

The three most common methods used to assess fatigue intensity and obtain a quantitative estimate of the severity of fatigue are the Verbal Rating Scale, the Visual Analogue Scale and the Numerical Rating Scale. The first scale to rate tiredness (in relationship to prolonged mental work) was developed in the 1920's by Poffenburger (1928). He used the following seven-point verbal rating scale to elicit how the subject was feeling:

1. Extremely good
2. Very good (as after a good night)
3. Good
4. Medium
5. Tired
6. Very tired
7. Extremely tired.

The self-report of fatigue intensity has been measured most frequently with the Feelings of Fatigue Scale (Yoshitake, 1971), Rhoten's Fatigue Scale (Rhoten, 1982) and Pearson and Byar's Fatigue Feeling Tone Scale (Pearson and Byars, 1956).

Pearson and Byars (Pearson and Byars, 1956 ; Pearson, 1957) reported the development of a ten-item unidimensional scale measuring the subjective quality of tiredness in relationship to psychomotor tasks in airmen. This was later used in several nursing studies (Hart, 1978 ; Haylock and Hart, 1979 ; Davis, 1984 ; Rieger, 1987 ; Cohen and Hardin, 1989 ; Srivastava, 1989). This ten-item adjective list (figure 3.1) defined the fatigue level continuum in short, easily understood phrases, composed of equidistant adjacent items. Each adjective is scored in relation to whether the person at that time felt better than, the same as, or worse than that specific feeling. Weighting categories (*better than* as one, *same as* as two and *worse than* as three) provides a score that increases as fatigue increases. An initial set of five hundred adjectives were selected. Subsequent studies led to the elimination of those items with low validity and internal consistency. The remaining ninety-two items were scaled using Thurstone's method of equal appearing intervals. Two equivalent forms of the checklist were ultimately constructed. The equivalent forms show high intercorrelation (r= .92) both for one hundred experimentally fatigued subjects and for one hundred control subjects. The checklist clearly differentiated between the experimentally fatigued subjects and the control subjects over time.

Figure 3.1 Pearson-Byars Fatigue Feeling Tone Checklist

Number	Better Than	Same As	Worse Than	Statement
1.	( )	( )	( )	Very lively
2.				Extremely tired
3.				Quite fresh
4.				Slightly pooped
5.				Extremely peppy
6.				Somewhat fresh
7.				Petered out
8.				Very refreshed
9.				Fairly well pooped
10.				Ready to drop

Source: Pearson, R. (1957). Scale analysis of a fatigue checklist. Journal Of Applied Psychology, 41, (3), p.188.

Their interval scale represents the most thorough effort to devise a measure of subjective fatigue as a unidimensional feeling of tiredness. Limitations include the colloquial content of the checklist, the underlying assumption that fatigue is an overall

feeling of unidimensional unpleasantness, and lack of validity and reliability estimates to indicate that this instrument, originally designed to measure fatigue in airline pilots, measures tiredness in patient populations, although its authors suggest that its applicability should be general.

Yoshitake (1971) developed a nine-point scale for subjects to rate their feelings of fatigue ranging from (1) "feeling fit, rested" to (9) "feeling extremely tired, exhausted". The intermediate points were indicated by numerical ratings only. The Rhoten Fatigue Scale (Rhoten, 1982) is a subjective rating to be used by the patient to quantify fatigue (figure 3.2). The scale was employed to correlate the level of fatigue assigned from an objective observation checklist and patients' subjective feelings. Rhoten has not reported reliability and validity for these scales although correlations were observed between the rankings on both scales. However, a small number ($n = 5$) of patients participated in

Figure 3.2 Rhoten Fatigue Scale and Observation Checklist

Observation Checklist

CATEGORY	SUB-CATEGORY	DESCRIPTORS
1.General Appearance	Physical appearance	5
	Colouring	4
	Breathing	8
2.Communication	Eyes	6
	Facial Expression	8
	Speech	11
3.Activity	Movements	4
	Ambulation	4
	Posture	7
	Food and fluid intake	6
4.Attitude	Attitude	11

Rhoten Fatigue Scale

0 1 2 3 4 5 6 7 8 9 10

Not tired
Full of energy
Peppy

Total exhaustion

Source : Rhoten, D. (1982). Fatigue and the post surgical patient. In C Norris (Ed.), Concept Clarification in Nursing, p 289 and 291. Rockville, Maryland; Aspen Systems Corporation.

the study . It has been used in a range of nursing studies (Blesch, Paice, Wickham, Harte, Schnoor, Purl, Rehwait, Lamm Kopp, Manson, Barry Coveny, McHale and Cahill, 1991 ; Gardner, 1991 ; Pickard-Holley, 1991).

The first tool provides interval definition with adjectives, but the colloquial content of the list limits its use. A major limitation of the latter tools, which use numerical incremental scales, is the lack of definition of the intervals. They provide a way of measuring change in a patient's fatigue intensity level, however, they would not allow comparisons between patients.

Cardenas and Kutner (1982) in a study of fatigue in patients receiving maintenance dialysis for renal insufficiency, employed a simple linear scale with a line ranging from zero to one hundred, with zero corresponding to total exhaustion, 25 = very tired, 50 = mediocre, 75 = good, and 100 = great (no fatigue at all). Validity and reliability were not explored, but in a study by Srivastava (1989) results obtained were supported by a variety of instruments used in the quantification of the fatigue experience.

Crosby (1991) suggested using techniques such as magnitude estimation. This would involve asking subjects to indicate the least amount of fatigue over the past week and then indicating the level of fatigue they were experiencing at the time of the study. This *floating* baseline would allow for differences in the magnitude of fatigue to be assessed.

Schaefer and Potylycki (1993) have explored the validity of a number of rating scale approaches in the measurement of fatigue intensity. Participants with congestive heart failure were asked to rate fatigue on the visual analogue scale (VAS), a graphic rating scale (GRS, verbal descriptors are not reported) and a numerical rating scale (NRS) from one to ten. Moderately high significant correlations supported the validity of each of these tools ; VAS and GRS, $r = .65$, $p < .01$; VAS and NRS, $r = .77$, $p < .01$; GRS and NRS, $r = .68$, $p < .01$.

Lee, Hicks and Nino-Murcia (1991) developed an eighteen-item bipolar visual analogue scale (VAS-F) to evaluate levels of fatigue and energy then tested it in healthy adults with no complaints of chronic fatigue or sleep disorders and in patients undergoing evaluation at a sleep disorders clinic (figure 3.3). Descriptors were obtained from the literature and from content analysis of personal interviews with patients complaining of fatigue. The scale compared favourably with the Profile Of Mood States (POMS) and the

Figure 3.3 Visual analogue scale for fatigue

1.	Not at all tired	_____	extremely tired
2.	Not at all sleepy	_____	extremely sleepy
3.	Not at all drowsy	_____	extremely drowsy
4.	Not at all fatigued	_____	extremely fatigued
5.	Not at all worn out	_____	extremely worn out
6.	Not at all energetic	_____	extremely energetic
7.	Not at all active	_____	extremely active
8.	Not at all vigorous	_____	extremely vigorous
9.	Not at all efficient	_____	extremely efficient
10.	Not at all lively	_____	extremely lively
11.	Not at all bushed	_____	extremely bushed
12.	Not at all exhausted	_____	extremely exhausted
13.	Keeping my eyes open is no effort at all	_____	keeping my eyes open is a tremendous chore
14.	Moving my body is no effort at all	_____	moving my body is a tremendous chore
15.	Concentrating is no effort at all	_____	concentrating is a tremendous chore
16.	Carrying on a conversation is no effort at all	_____	carrying on a conversation is a tremendous chore
17.	I have absolutely no desire to close my eyes	_____	I have a tremendous desire to close my eyes
18.	I have absolutely no desire to lie down	_____	I have a tremendous desire to lie down

Items 1-5 and 11-18 belong to the fatigue subscale. Items 6-10 belong to the energy subscale.

Source: Lee, K., Hicks, G. and Nino-Murcia, G. (1991). Validity and reliability of a scale to assess fatigue. Psychiatry Research, 36 p. 294.

Stanford Sleepiness Scale (Hoddes, Zarcone, Smythe, Phillips and Dement, 1973). Internal consistency, reliability and sensitivity were high.

Wood (1990) measured peoples differing energy levels (physical and mental) in particular vigour, vitality and fatigue. Healthy volunteers took part in interviews exploring their experiences of physical and mental energy. Particular attention was given to work-related factors and energy levels. He used two visual analogue scales, one for physical energy, and one for mental energy and the POMS. The scales were successful in charting changes in physical and mental energy over the course of a week. Also individuals showed different patterns of fluctuation in energy throughout the day. There was a strong connection between feeling energetic and feeling well in general.

Numerous researchers have utilised the visual analogue scale to elicit the degree of fatigue experienced during illness (Krupp, Alvarez, LaRocca *et al.*, 1988 ; Tack, 1990c ; Crosby, 1991). There are many advantages and limitations to the use of visual analogue scales and the variant verbal graphic rating scale(see Chapter 5). During pain assessment in the clinical setting the most common methods approach equivalency (Jensen and Karoly, 1992), and the techniques utilised in examining the reliability, sensitivity and validity of such tools could be usefully transferred to the quantification of severity of fatigue . Attention needs to be directed at achieving consistency in the selection of endpoint statements. A scale that measures fatigue should employ descriptive adjectives that represent both extremes of a continuum and it should be ensured that scales consist of adjectives at each extreme representing the same continuum. Researchers should explore the orientation (vertical versus horizontal) of the visual analogue scale capable of achieving the most reliable and sensitive results. Lee (1990) following some preliminary cross-cultural research exploring the sensitivity, reliability and validity of horizontal and vertical VASs and five-point and seven-point verbal descriptive scales concluded that the use of the VAS constituted the more sensitive approach. Consideration should also be given to the likelihood that a simple unidimensional scale may provide useful information, yet may also be limited with regard to representative richness of subjective experience of fatigue.

3.7.2 Assessing fatigue characteristics

There is evidence of sensory, temporal, affective/emotional, and evaluative components of fatigue which are conceptually and empirically distinct from fatigue intensity. These discrete dimensions may be defined as the bodily feelings, trends experienced, emotional feelings, and disruption engendered by the fatigue experience, whereas fatigue intensity

may be defined as the amount of fatigue experienced. Because people's feelings about events can be mixed, it is likely that the domain of subjective fatigue consists of multiple dimensions, which may be closely related to one another. The dimensions require clarification and then translation into scale items susceptible to quantification. It is still unclear whether subjective fatigue is best assessed as a single domain, multiple dimensions or may be reliably assessed as both a global construct and a set of related dimensions. Its complex nature suggests that single-item measures may be less reliable than multiple item measures. Scales which are unidimensional will not explore the composite nature of the concept . However, depending on the specific items included, even multiple-item measures may assess only a limited number of the dimensions associated with fatigue. This is a more complex dimension than fatigue intensity and fewer measures are available to measure this construct.

A number of terms are in common use which refer to fatigue. Individuals may complain of being tired, drowsy, needing more sleep, lacking vigour or vitality, feeling weak, having decreased energy or strength, and feeling unable to complete certain activities. Physically people may say they are weak all over , point to weakness in a particular muscle group, or say they lack strength, power or feel tired.

Specific measurement studies have been conducted to identify sets of symptoms that can be grouped together into categories using factor and key cluster analysis. Kinsman and Weiser (1976) provide a detailed account of such studies in relationship to work and fatigue. They applied the multidimensional analysis of subjective symptomatology to a standard work situation on the bicycle ergometer in controlled laboratory conditions (Kinsman, Weiser and Stamper, 1973). In this study, four stages were involved in the development of a Physical Activity Questionnaire designed to describe categories of subjective symptoms experienced as a result of prolonged bicycle riding.

- Items were selected from an Initial Adjective Checklist assembled from previous reported measures of fatigue
- Each descriptive item was arranged along a five-point ordinal scale of severity
- Sixty-four subjects, on two occasions at least three days apart rode the bicycle ergometer. The instrument was presented to the subjects at various intervals.
- Items which were redundant or showed less than a 10% mean change from pre- to end-of-ride were eliminated.

A number of key cluster analyses were then performed. Three symptom categories were identified and labelled on a conceptual basis - Fatigue, Task Aversion and Motivation. The fatigue category appeared to be composed of those subjective symptoms

describing bodily feeling states associated with prolonged exercise (Kinsman, Weiser and Stamper, 1973). In a subsequent study (Weiser, Kinsman and Stamper, [1973] cited in Kinsman and Weiser [1976]) two subcategories of fatigue were identified and labelled General Fatigue and Leg Fatigue. It seemed to represent a truly general type of subjective fatigue, common to different tasks, environmental conditions (Stamper, Kinsman and Evans, 1970 ; Stamper, Sterner and Kinsman, 1971), and pathology (Kinsman, Luparello, O'Banion *et al.*, 1973 ; Kinsman, O'Banion, Resnikoff *et al.*, 1973). On the other hand leg fatigue is a symptom subcategory apparently specific to tasks that are very much dependent on their use e.g. bicycling.

The thirty-item Fatigue Symptom Checklist, developed under the auspices of the Japanese Industrial Fatigue Research Committee Of The Japanese Association Of Industrial Health, proposed in 1967 derived from an earlier version in 1954 (Yoshitake, 1969 ; Kogi, Saito and Mitsuhashi, 1970 ; Saito, Kogi and Kashiwagi, 1970 ; Yoshitake, 1971 ; Yoshitake, 1978), is another example of such an approach. This checklist has been used in several nursing studies (Hart, 1978 ; Haylock and Hart, 1979 ; Davis, 1984 ; Srivastava, 1989).

An initial inventory was formulated on a conceptual rather than an empirical grouping in 1954. During the late sixties and early seventies the items of the inventory were used to develop the scale by factor analytic techniques and the validity of the suggested items was investigated by Kogi, Saito and Mitsuhashi (1970). A description of further empirical work leading to the derivation of the scale is presented by Saito,Kogi and Kashiwagi (1970). The result of this work was a thirty-item fatigue symptom checklist containing three dimensions or categories:

- The first symptom dimension was described as a dull, sleepy factor, representing general feelings of incongruity in the body. Symptoms in this category included heaviness in the head, tiredness in the body and tired legs.

- The second dimension pertaining to a decline in motivation to work was composed of mental symptoms that appear to lack physical basis. Symptoms included were difficulty in thinking, weariness while talking, nervousness, inability to concentrate and forgetfulness.

- The third dimension pertained to projections of fatigue to specific parts of the body or feelings of incongruity in specific body parts. Included in this dimension were headache, stiff shoulders, dizziness and tremor in limbs.

These dimensions and their representative items are shown in figure 3.4. The frequency of complaints of fatigue can be calculated by counting the number of checked items. Discovery of differences in the factorial structure in relationship to different groups of workers suggests that specific symptoms and symptom categories may not apply in the evaluation of fatigue in certain work situations and hence casts doubt on the usefulness of this tool in other settings. Additionally the symptom factors were based on frequency rather than severity and thus intensity of complaints cannot be inferred. However, when Yoshitake (1971) investigated the relationship of these symptoms to levels of fatigue among bank workers and broadcasting workers he found that the correlation between frequency of complaints of symptoms of fatigue and the feeling of fatigue was extremely high. However, the degree of sensation varied for different types of symptoms. In this healthy worker population, which included industrial shift workers, bankers, and secretaries, feelings of general incongruity were almost always present in states of fatigue regardless of work type.

Limitations of the checklist include the underlying assumption that the feeling of fatigue is unpleasant and that frequency and intensity are linearly related; it was developed to measure industrial fatigue occurring in relationship to physical and mental work in normal subjects. Items purporting to describe symptoms of fatigue may not be similar to those symptoms that are experienced by the chronically ill. Whether a tool developed and tested on a population of healthy Japanese workers would transfer to other cultures and acute and chronically ill subjects could be questioned (Varricchio, 1985). Cultural differences may influence the validity of this instrument. There is a need to document the relationship between these symptoms of fatigue and specific pathologies and identify whether fatigue is manifested the same way in healthy and sick individuals. The symptom patterns may vary according to illness. Berrios (1990) argues that if the feeling of fatigue constitutes a primary feeling-state, irrespective of whether it is preceded by exertion, we can hypothesise that it should be the same for all clinical situations : i.e. the fatigue of multiple sclerosis should be the same as that for cancer, or renal disease. This question must be answered by empirical research, for which a suitable evaluative instrument is required.

Krupp, LaRocca, Muir-Nash and Steinberg (1989) developed a fatigue severity scale (figure 3.5), subjected it to tests of internal consistency and validity, and used it to compare fatigue in two chronic conditions : systemic lupus erythematosus (SLE) and

Figure 3.4 Fatigue Symptom Checklist

A. General Feeling Of Incongruity

1. Feel heavy in the head
2. Feel tired in the whole body
3. Feel tired in the legs
4. Give a yawn
5. Feel the brain hot or muddled
6. Become drowsy
7. Feel strained in the eyes
8. Become rigid or clumsy in motion
9. Feel unsteady while standing
10. Want to lie down

B. Mental Symptoms

11. Find difficulty in thinking
12. Become weary while talking
13. Become nervous
14. Unable to concentrate attention
15. Unable to have interest in thinking
16. Become apt to forget things
17. Lack of self-confidence
18. Anxious about things
19. Unable to straighten up in posture
20. Lack patience

C. Specific Feelings Of Incongruity

21. Have a headache
22. Feel stiff in the shoulders
23. Feel a pain in the waist
24. Feel constrained in breathing
25. Feel thirsty
26. Have a husky voice
27. Have dizziness
28. Have a spasm of the eyelids
29. Have a tremor in the limbs
30. Feel ill

Source: Yoshitake, H. (1971). Relations between the symptoms and the feelings of fatigue. Ergonomics, 14 (1), p.177.

Figure 3.5 Fatigue Severity Scale

	Statement*
1.	My motivation is lower when I am fatigued
2.	Exercise brings on my fatigue
3.	I am easily fatigued
4.	Fatigue interferes with my physical functioning
5.	Fatigue causes frequent problems for me
6.	My fatigue prevents sustained physical functioning
7.	Fatigue interferes with carrying out certain duties and responsibilities
8.	Fatigue is among my three most disabling symptoms
9.	Fatigue interferes with my work, family, or social life

* Patients are instructed to choose a number from 1 to 7 that indicates their degree of agreement with each statement where 1 indicates strongly disagree and 7, strongly agree.

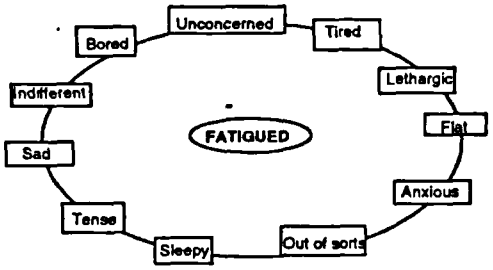
Source: Krupp, L., La Rocca, N., Muir-Nash, J. and Steinberg, A.(1989).The Fatigue Severity Scale. Application to patients with multiple sclerosis and systemic lupus erythmatosus. Archives of Neurology, 46,p. 1122.

multiple sclerosis (MS). Results revealed that the scale was internally consistent, correlated well with visual analogue measures and could detect clinically predicted changes in fatigue over time. It is a nine-item fatigue questionnaire developed from factor and item analysis and theoretical considerations and selected on the basis of ability to identify common features of fatigue in both MS and SLE. Subjects read statements and choose numbers from one to seven that best describe their degree of agreement - a Likert-type scale. A criticism of this scale is that most items are related to the behavioural consequences of fatigue rather than the symptoms themselves and the development of the scale centred around an extremely small sample.

The Feelings Of Fatigue Scale is currently under development (Berrios, 1990). It is a somewhat erratic collection of items and methods of measurement entailing the choice of two referents to time, now and within last month. This may be confusing for subjects. Examples of items are displayed in figure 3.6. It is at present undergoing validity and reliability testing (Berrios, Personal Communication 1993). It differs from other instruments in that its purpose is to identify semantic maps for different groups of the population. It is anticipated that maps would be stable over time, related to enduring behavioural and motivational styles and hence reflect trait rather than state aspects of a *biological personality*.

Figure 5.6 Representative items from the feelings of fatigue scale

PLEASE LINK BY LINES THE STATES YOU TEND TO EXPERIENCE TOGETHER WITH THE FEELING OF FATIGUE (maximum of 5)



THE FOLLOWING SITUATIONS WOULD MAKE ME FEEL:

(please mark more than one if required of those items that apply to your sex)

Irritable Sad Angry

I have been working very hard

WHEN I AM TIRED AFTER A HARD DAYS WORK I BECOME:

ALWAYS

NEVER

IRRITABLE

I TIRE EASILY, AND WHEN WORKING I HAVE TO STOP AND REST EVERY FEW MINUTES

never rarely occasionally often always

Source: Berrios, G. (1993) The Feeling of Fatigue Scale, 2nd Version. Personal Communication

A British team interested in chronic fatigue syndrome has developed a self rating scale to measure the severity of fatigue. It is intended to detect fatigue and symptom severity in epidemiological studies in primary health care populations (Chalder, Berelowitz, Pawlikowska, Watts, Wessely, Wright and Wallace, 1993). A fourteen item Likert scale (depicted in figure 3.7) reflecting physical and mental fatigue was generated. Principal components analysis suggested that the scale consisted of these two constructs. A high level of internal consistency was obtained both for the scale as a whole and its subscales. There was also strong evidence of discrimination. The scale is based on similar questionnaires designed for a hospital based case control study and a treatment outcome study (Wessely and Powell, 1989 ; Butler, Chalder, Ron and Wessely, 1991). A shorter modified version of this original questionnaire was utilised in a community study examining the prevalence and associations of symptoms of fatigue - the researchers eliminated all but one of mental fatigue items, retaining the item related to concentration (David, Pelosi, MacDonald *et al.*, 1990). The variable inclusion of items and differing response format limit the contribution of these studies in supporting the validity of the tool. Of concern is the age spread of the subjects: eighteen to forty-five years. This does not reflect the preponderance of the elderly in the population at present. Further testing would need to be undertaken ensuring adequate representation of this group.

Figure 3.7 Fatigue Scale

Physical Symptoms

1. Do you have problems with tiredness?
2. Do you need to rest more?
3. Do you feel sleepy or drowsy?
4. Do you have problems starting things?
*5. Do you start things without difficulty but get weak as you go on?
6. Are you lacking in energy?
7. Do you have less strength in your muscles?
8. Do you feel weak?

Mental Symptoms

9. Do you have difficulty concentrating?
10. Do you have problems thinking clearly?*
11. Do you make slips of the tongue when speaking?
12. Do you find it more difficult to find the correct word?
13. How is your memory?
14. Have you lost interest in the things you used to do?*

Subjects respond by selecting one of the following responses "better than usual", "no more than usual", "worse than usual" or "much worse than usual".
* denotes items omitted in revised version.

Source : Chalder, T., Berelowitz, G., Pawlikowska, T., Wright, D., Wallace, P., Wessely, S. The development of a fatigue scale. Journal Of Psychosomatic Research, 37 (2), p.153.

The Piper Fatigue Scale incorporates a range of diagnostic dimensions and is designed to measure change in fatigue patterns in ill populations (Piper, Lindsey, Dodd *et al.*, 1989). The items and dimensions were not empirically derived but guided by the clinical expertise of the authors and by the literature on the conceptualisation and measurement of symptoms. It is a tool designed for research and not clinical assessment and is examined in further detail in Chapter 5. This instrument has been evaluated with a relatively small number of patients with cancer, and more data are required to evaluate its psychometric properties and applications with confidence. The total fatigue score is calculated on the basis of the scores from four subscales representing the temporal, intensity, affective and sensory dimensions of fatigue (see figure 3.8). No mention is made whether the assumed dimensions of fatigue are reflected in the patient population.

Figure 3.8 Piper Fatigue Scale - subscales with a representative item

Temporal Dimension

To what degree has your fatigue changed in the past week?

Decreased_____Increased

Severity/Intensity Dimension

How severe is the fatigue which you are experiencing now?

No fatigue_____Worse fatigue

Affective Dimensions

To what degree would you describe the fatigue you are experiencing now as being

Normal_____Abnormal

Sensory Dimension

To what degree are you are now feeling alert

Alert_____Drowsy

Source : Piper, B., Lindsey, A., Dodd, M., Ferketich, S., Paul, S., Weller, S. (1989). The development of an instrument to measure the subjective dimension of fatigue. In S. Funk, E. Tornquist, M. Champagne, L. Copp, R. Wiese (Eds.), Key Aspects Of Comfort, p.201. New York, New York: Springer Publishing Company.

The Multidimensional Assessment Of Fatigue (MAF) contains sixteen items and measures four dimensions of fatigue : severity, distress, timing, and degree of

interference in activities of daily living (Tack, 1990c). Fourteen items are VASs and two items have multiple choice responses. Respondents are asked to reflect on fatigue patterns for the past week. Scoring the MAF results in the Global Fatigue Index, which ranges from zero (no fatigue) to five hundred (extreme fatigue). Psychometric properties of the MAF have been documented. Cronbach's alpha is .93 and Pearson's correlations indicate the MAF has convergent validity with the POMS fatigue subscale (r= .78, p< .001) and has divergent validity with the POMS vigour subscale (r= .60, p< .001). The MAF is short, easy to complete and could be used in a clinical situation for multiple purposes: assessment of baseline reports of fatigue, effects of therapeutic interventions aimed at ameliorating fatigue and monitoring the natural course of an illness in relationship to fatigue. It was used in a study by Belza, Henke and Yelin *et al.* (1993), however, further validity and reliability data were not offered by the researcher on this occasion.

Tack (1990a) describing the multidimensional nature of the fatigue experience for individuals with rheumatoid arthritis developed The Fatigue Interview Schedule (see figure 3.9). This is a fifteen-item, semi-structured interview which includes predominately

Figure 3.9 Fatigue Interview Scale

1. Describe/define what your fatigue is like
2. Do you have feelings that tell you that you are becoming fatigued? If yes, what are they?
3. What typically brings your fatigue on?
4. How often does your fatigue occur? (e.g.. every afternoon, weekends only)
5. How long does your fatigue last? (e.g.. 2 hours, 3 days)
6. When you are fatigued, what other physical sensations do you notice?
7. When you are fatigued, what emotions or feelings do you notice?
8. What is the most bothersome thing about being fatigued?
9. Does your fatigue ever lessen or go away? If yes, what do you do to help the fatigue become less or go away? Does it make the fatigue go away entirely?
10. What types of things do others do to decrease your fatigue or make it go away? Does it make the fatigue go away entirely (e.g.. degree of effectiveness)?
11. Did you experience fatigue before you were diagnosed with arthritis? If yes, was the fatigue different than the fatigue you experience now? If yes, how?
12. How has fatigue affected your relationship with your friends? with family? with co-workers?
13. Do you feel people believe you are fatigued when you say you are? If no, explain.
14. How would someone know that you are fatigued?
15. Is there anything I did not ask you about fatigue that you want to tell me?

Source: Tack, B. (1990a). Fatigue in rheumatoid arthritis. Arthritis Care And Research, 3 (2), p. 67.

open questions relating to the respondent's perception of fatigue, it's aggravating and alleviating factors and prodromal indicators. Information about adaptive mechanisms and effects of fatigue on activities of daily living was also obtained. An instrument with similar content has recently been developed, the Analysis Of High Intensity Self-Care Needs And Interventions Survey (Robinson and Posner, 1992), but reliability and validity data have not been obtained for this tool.

The inductive approach in the development of a theoretical model through which to develop measuring instruments is innovative and should be pursued more vigorously. Crucial domains which emerge for the differing sample groups may be identified by adopting such a methodology. The characteristics of subjective fatigue have been viewed as difficult to measure adequately and consequently neglected. Many inadequacies in methodology are still evident and there is a paucity of well directed and systematic investigations.

3.7.3 Assessing the impact of fatigue

The degree to which fatigue impinges on other areas of a person's life is an important consideration. Instead of obtaining an estimate of fatigue perception itself, various instruments have been developed to measure the consequences of fatigue, the impact of fatigue on performance or fatigue as a component of depression or other symptomatology. Additionally, the subjective feeling of fatigue is often a concept incorporated into tools which measure a broader, more diverse set of concepts or constructs.

An understanding of the significance of fatigue in the daily life of patients requires identification of the range of symptoms associated with fatigue. There may be similarities as well as differences in the symptoms in different patient populations. These symptoms may reflect the subjective or objective characteristics of patients. Objective characteristics include sleep and exercise performance as well as job or role performance. Several recent studies have explored the correlates of fatigue in various populations. For example, Srivastava (1989) reports a negative correlation between fatigue and subjective quality of life in patients in the terminal stages of renal disease. Although this relationship is intuitively expected, its statistical strength suggests the importance of fatigue in the total life experience of these patients.

3.7.3.1 Quality of life

The impact of fatigue on quality of life requires investigation. Several authoritative reviews on the measurement of quality of life in cancer patients exist (Goodinson and Singleton, 1989 ; Hawthorn, 1993 ; Selby, 1993). A number of domains have been identified repeatedly as minimum requirements for a quality of life instrument. Measurement usually involves the evaluation of physical functioning, psychological status, social relationships and symptom domains that will interact with fatigue. A crucial function of quality of life scales has been the identification of distressing symptoms or side-effects associated with the disease or its treatment. Tiredness and lack of energy are frequently addressed.

Instruments are cancer/disease specific or dimension specific. A number of cancer/disease specific instruments exist and a brief description of three such instruments follows. The Quality Of Life Index developed by Padilla, Presant, Grant, Metter, Lipsett and Heide (1983) includes three general areas: psychological well-being (general quality of life, fun, satisfaction, usefulness, sleep), physical well-being (strength, appetite, work, eating, sex), and symptom control (pain, nausea, vomiting). The EORTC-QLQ-C30 developed through the European Organisation For Research And Training In Cancer Quality Of Life (Aaronson and Beckman, 1987 ; Aaronsen, Ahmedzai, Bergman, Bullinger, Cull, Duez, Filiberti, Flechtner, Fleishman, de Haes, Kaasa, Klee, Osoba, Razavi, Rofe, Schraub, Sneeuw, Sullivan and Takeda, 1993) has twenty-eight items plus two global quality of life items. Disease or problem specific items are intended to be added to the scale. The measure has questions on physical abilities, symptoms, mood, cognitive function, social interactions and finances. The Linear Analogue Self Assessment (Priestman and Baum, 1976) evaluates ten areas of a cancer patient's life : feeling of well-being, mood, level of activity, pain, nausea, effectiveness of treatment, appetite, ability to perform housework, social activities and level of anxiety.

Instruments delineating single domains also exist. Domain specific approaches seek assessment of variables related to a multidimensional concept. These may be combined in multiple combinations to increase the depth and breadth of data obtained from single instruments. Employing increasingly sensitive measures for specific domains may become more feasible with the use of multiple instruments. Those commonly involved in measuring elements of quality of life and in the study of fatigue are briefly considered below.

3.7.3.2 Psychological distress and well-being

Although not easily measured, the psychological component of fatigue should be taken into consideration. When fatigue is discussed in terms of its psychological aspects, the focus is usually on the relationship between fatigue and stress, depression, anxiety and motivation.

Among the many symptoms possible during a chronic illness such as cancer, mood disorder represents one of the most difficult to identify. This stems from the similarity of presentation of some mood symptoms and common disease complaints, such as fatigue, sleep disruption and loss of concentration.

Many well standardised, psychometrically sound measures are available to measure mood and diagnose specific mental disorders. For assessing anxiety the State-Trait Anxiety Inventory (Spielberger, Gorsuch and Lushene, 1970) is the most widely used and provides self-report measures of both state and trait anxiety as a means of measuring psychological well-being. The Beck Depression Inventory (BDI) is one of the more commonly used measures of the construct of depression (Beck, Ward, Mendelson, Mock and Erbaugh, 1961). The Brief Symptom Inventory (BSI) (Derogatis and Melisaralos, 1983) , the brief form of the SCL-90-R (Derogatis, Rickels and Rock, 1976) is a fifty-three item self-report symptom inventory designed to measure current psychological status along a number of dimensions (nine subscales) which include anxiety, depression, somatization and hostility. It was designed for use with psychiatric and medical patients as well as healthy subjects. Understanding emotion in relation to behaviour requires the inclusion of subjective data of feeling, affect, and mood. To meet this need McNair, Lorr and Droppleman (1992 revised) developed the Profile Of Mood States (POMS). This is a self-administered scale measuring six mood or affective states : tension-anxiety, anger-hostility, vigour-activity, fatigue-inertia, confusion-bewilderment, and depression-dejection.

It can be difficult, if not impossible to be certain of the aetiology of somatic symptoms. An awareness that instruments which entail inclusion of physical items of depression and anxiety which overlap with the common symptoms of some chronic conditions such as cancer should be maintained. The Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983) is often recommended to overcome this problem.

Clinically and socially relevant changes in mental health are not always captured by measures of psychological distress (Ware Jr., 1991). Accurate documentation of the

feeling that life is less enjoyable, the person is less happy or cheerful require items that assess psychological well-being as well as psychological distress. Investigators should consider whether the instrument selected is sensitive to levels of well-being in those free of psychological distress.

3.7.3.3 Social support and interaction

Social relationships are acknowledged as crucial to the functioning and well-being of people with chronic illness. Emotional, informational and physical support as well as social environment are important considerations. Social support instruments have been reviewed by Lindsey (1992) . The Norbeck Social Support Questionnaire (Norbeck, Lindsey and Carrieri, 1981) is one such instrument designed to measure the multidimensional construct of social support.

The quality and availability of social support may have an important role to play in the recovery processes during and following an illness. Loss or lack of social support may in future be shown to be related to fatigue and the ability to cope with it. Social support may have a protective function mediating the effects of stressful life events and buffering against stressful circumstances or crises. If in fact social support is a moderating variable influencing the maintenance of health and health outcomes, determining the level of perceived social support, the availability of support, and changes in support over time will become important clinical considerations. Enhancing or facilitating the quality or quantity of social support may be a crucial intervention strategy throughout the illness and treatment trajectory in the amelioration of fatigue.

3.7.3.4 Concurrent symptoms

There has been increasing interest in the measurement of symptom occurrence and symptom distress during illness. Many instruments have been developed to measure symptoms, including tiredness associated with a variety of clinical problems, and several have been specifically designed for use with cancer patients.

The Symptom Profile Instrument (King, Nail, Kreamer, Strohl and Johnson, 1985) was developed to document the occurrence of symptoms experienced by cancer patients during treatment. The list of thirteen symptoms includes fatigue. The severity rating is made on a Likert-type scale of not bad, a little bad, moderately bad, quite bad, and extremely bad. The Symptom Distress Scale (McCorkle and Young, 1978) measures

fatigue on a five-point scale with the anchors "Could not feel more tired" (5) to "I am not tired at all" (1). Subjects were asked to put a circle around the number that most closely measured how they perceived the amount of fatigue distress at that moment in time or for that day. In a subsequent investigation (Donaldson, McCorkle, Georgiadou and Quint Benoliel, 1986) the scale was modified and descriptive words for each numerical indicator were added. Fatigue indicators were (1) "I am usually not tired at all"; (2) "I am occasionally rather tired"; (3) "There are frequently periods when I am quite tired"; (4) "I am usually very tired" and (5) "Most of the time I feel exhausted". More recently the Rotterdam Symptom Checklist (de Haes, Van Knippenberg and Neijit, 1990) has been developed which includes items that refer to feeling tired, having sore muscles and lacking in energy.

3.7.3.5 Function

There has been increasing interest in the measurement of functional status during illness. Physical functioning and functional status are terms which are used interchangeably and equated with health status and level of impairment. It is vital to explore the relationship of functional status to fatigue. Nurses can assist patients to maintain or improve functional status in the light of fatigue. Researchers may measure the level at which a person is functioning in a variety of areas, such as physical health, work activity, social activity, self-care ability and emotional status. This dimension of quality of life has been reviewed thoroughly (McMillen Moinpour, McCorkle and Saunders, 1992).

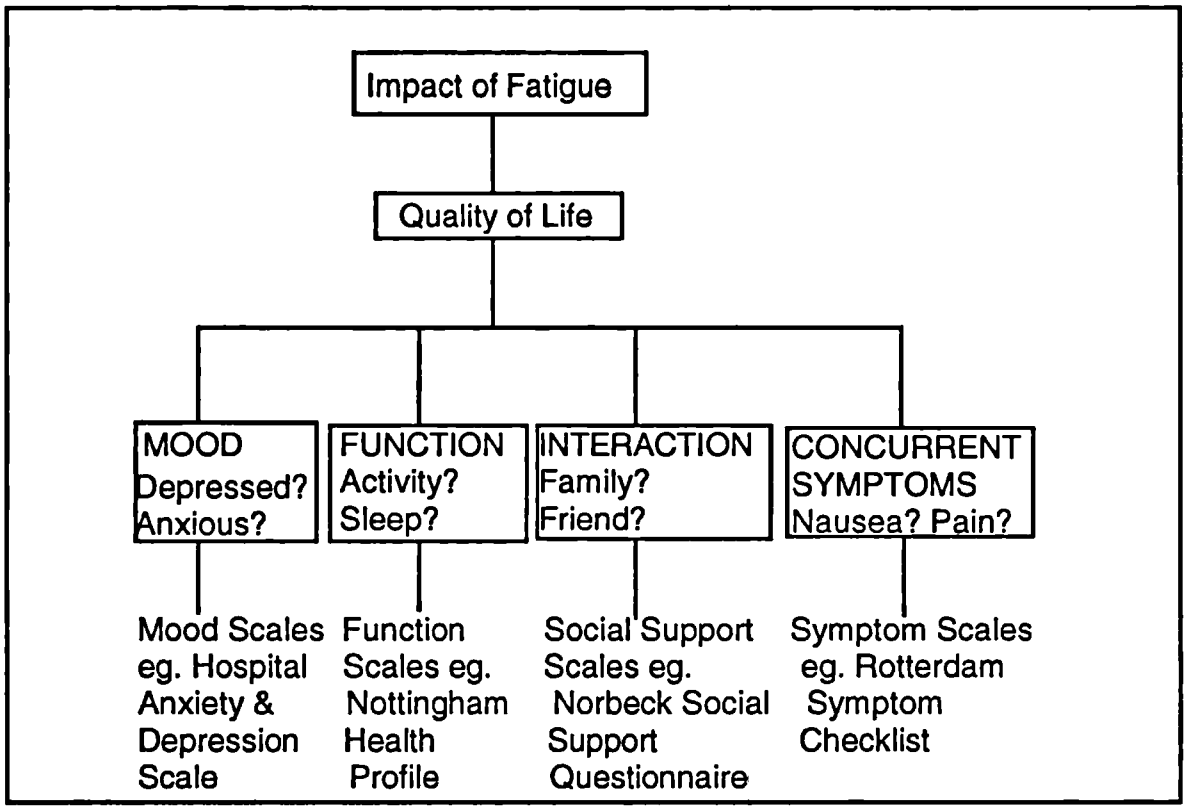
Physical performance scales exist for the adult cancer patient and can be used to assess current level of functioning. The Karnofsky Performance Status Scale (Karnofsky and Burchenal, 1949) and the Eastern Co-operative Oncology Group Zubrod Scale are two such instruments. However, the physician's assessment may be different from the patient's own assessment on this scale. The Zubrod Scale (a scale of zero to four in increments of one) evaluates the ability of the patient to remain ambulatory and perform activities of living (Zubrod, Schneiderman, Frei, Brindley, Gold, Shnider, Cviedo, Gorman, Jones, Jonsson, Colsky, Chalmers, Ferguson, Dederick, Holland, Selawry, Regelson, Lasagna and Owens, 1960). Karnofsky developed a scale which rates physical activity from one percent to one hundred percent in increments of ten percent. It, too, is an observer-rated tool developed to describe the functional status of cancer patients in response to the impact of disease and treatment. They reflect medical physical aspects of illness rather than the overall functional state. The Functional Living Index - Cancer (Schipper, Clinch, McMurray and Levitt, 1984) has five factors with a total of twenty-two items : physical well-being, psychological status, family situational interaction, social

ability and somatic sensation. It is an example of an instrument developed largely in response to the criticisms of previous tools. It is cancer specific and determines the patient's functional response to their illness and treatment. The measure is sufficiently specific to detect differences in functional status among patients in a different disease group.

Broad ranging generic instruments include the Nottingham Health Profile (Hunt, McKenna, McEwen, Williams and Papp, 1981) and the Symptom Impact Profile (Bergner, Bobbitt, Pollard, Martin and Gilson, 1976 ; Bergner, Bobbit, Carter and Gilson, 1981) Health status areas of the former include physical mobility, pain, sleep, emotional reactions, social isolation and energy. The categories of the latter are physical (body movement, mobility, ambulation), psychosocial (intellectual function, social interaction, emotional behaviour, communication) and sleep and rest, nutrition, usual daily work, household management, leisure and recreation. The subject's view of their limitations in physical activities owing to health problems can also be measured by the Physical Functioning Scale, a component of the Medical Outcomes Study Short Form Health Survey (Stewart, Hays and Ware, 1988) . This ten-item scale includes the concepts of self-care, mobility, ambulation, and varying degrees of physical activity and vitality.

Fatigue or aspects of fatigue and its potential impact on quality of life has been measured as a component of several instruments, some of which have been detailed briefly. Figure 3.10 summarises some of the relationships to the construct of fatigue. In the future preventive interventions will need to be developed to delay or offset the impact of fatigue on the daily life of patients. The range of reactions to fatigue and the situations which exacerbate or alleviate it should be detailed. This will only become possible with an acknowledgement of the likely relationships to the variables outlined previously.

Figure 3.10 Assessing the Impact of Fatigue



3.8 Physiological And Behavioural Indicators

Whilst measurement of the subjective nature of fatigue is primarily based on self estimation of the state of fatigue, assessment of objective manifestations of fatigue is even more difficult. Physiological, biochemical and behavioural measures have not been correlated systematically with subjective measures of fatigue. Further research is needed to clarify these relationships, particularly with different clinical populations.

3.8.1 Physiological and biochemical indicators

A variety of physiological indicators and methods have been used to study fatigue. Standard physiological stress tests such as cycle ergometry have traditionally been employed (Christensen, Bendix and Kehlet, 1982 ; Christensen, Nygaard and Kehlet, 1988). Heart rate, blood pressure, respiration and oxygen consumption may be recorded when monitoring the relationship of fatigue to exercise tolerance (Amundsen, 1979 ; Zeiderman, Welchew and Clark, 1990). Muscle function may be investigated with

electromyography (Malmquist, Ekholm, Lindstrom, Petersen and Ortgengren, 1981). To what extent such physiological changes occur in all instances of fatigue, such as the fatigue associated with physical exertion versus the fatigue associated with mental exertion remains to be investigated (Piper, 1986).

Several biochemical indicators and methods have been studied in relationship to exercise, but researchers have not always been able to demonstrate a relationship between fatigue and biochemical indicators. These include pH changes, skeletal muscle enzyme activity and metabolic substrates as exercise may induce fatigue by altering the concentration of skeletal muscle metabolites (Christensen, Nygaard and Kehlet, 1988 ; Christensen, Nygaard, Stage and Kehlet, 1990 ; Lewis and Haller, 1991 ; St.Pierre, Kasper and Lindsey, 1992). Mild adrenocorticol insufficiency has been suggested as a biochemical explanation for generalised fatigue (Poteliakhoff, 1981). Others that might be studied include rate and severity of anaemia, changes in levels of plasma glucose, thyroid hormones, serum electrolytes, and temperature changes. Anaemia is frequently associated with fatigue. However, this correlation has not been investigated. Documenting such a relationship between the clinical state, anaemia, and the phenomenon may depend on the rate of the decline in the haematocrit and haemoglobin values (Maxwell, 1984). It is hypothesised that the more quickly the decline occurs, the more profound the fatigue (Binder and Kales, 1979).

3.8.2 Behavioural indicators

Behavioural measures can be used by the nurse to monitor certain changes in physical functioning or activities. These may be helpful to determine changes that occur over time and those which may be specifically associated with fluctuating fatigue levels. These measures, as is true for the physiological measures, also may be influenced by factors other than fatigue. Lee (1990) draws attention to cultural differences in forms of fatigue expression. Whether subjective fatigue will be translated into fatigue behaviour will depend upon whether this is culturally acceptable or not.

Kashiwagi (1971) attempted to construct a fatigue rating scale through factor analysis techniques that would allow an objective evaluation of a person's appearance. He interpreted the Japanese Fatigue Symptom Checklist's dimensions as relating to : 1) weakened activation (dull, sleepy factor), 2) weakened motivation (mental symptoms), and 3) physical disintegration (specific feelings). Since he perceived the physical disintegration category as symptoms specific to specific types of work and the other two dimensions common to all kinds of work, he utilised only the first two dimensions and

twenty-eight additional items (see figure 3.11). He found that the component of weakened activation played the most important role in effectively being able to objectively evaluate changes in the level of fatigue. This scale has not been used by any other researcher.

Figure 3.11 Kashiwagi's Fatigue Rating Scale

Weakened Activation

1. Too lazy to walk
2. Unsteady voice
3. Absent minded
4. Hollow-cheeked
5. Avoid conversations
6. Sulky face
7. Spiritless eyes
8. Irritable
9. Listless face
10. Dull

Weakened Motivation

1. Many misstatements
2. Avoid others' eye
3. Difficult to speak to
4. Sluggish
5. Restless
6. Anxious about other things
7. Pale face
8. Stiff face
9. Trembling fingers
10. Unable to concentrate and listen

Items are checked as being present or not

Source : Kashiwagi, S. (1971). Psychological rating of human fatigue. Ergonomics, 14 (1) p.19.

Associating any consistent, overt physical behaviour with fatigue is difficult as the behavioural features which distinguish fatigued individuals are non-specific (Potempa, 1989). In general, patients complaining of fatigue tend to appear worn, wan, lethargic, and lacking in energy, and may exhibit a sagging face and body, lack of interest in surroundings and dull voice tones (Engle, 1970). Patients who complain of fatigue use such terms as *weary, tired, worn out, listless, no energy to carry on*, and express a strong desire to stop, lie down, or to sleep, in describing the subjective experience (Hart and Freel, 1982).

Nurses have identified behavioural indicators of fatigue (Freel and Hart, 1977 ; Putt, 1977 ; Rhoten, 1982) through behavioural checklists (Rhoten, 1982) and task

performance indicators (Heuting and Sarphati, 1966 ; MacVicar and Winningham, 1986). Rhoten developed an observation checklist and fatigue scale to clarify fatigue in post-operative patients. The checklist has four general categories with sub-categories and descriptors in each. These have been outlined in figure 3.2. It was based on objective observations and interviews, but with only five subjects. It has not been tested in other studies, but the categories, which include general appearance, communication, activity, and attitude, could be used to guide patient validated nursing assessments. Other nursing investigators have examined relationships between mental and physical fatigue and performance in card-sorting activity, standard neurocognitive tests and bicycling activities (Putt, 1977 ; MacVicar and Winningham, 1986 ; Cimprich, 1992).

3.9 Summary

It has been assumed that it is possible to measure human fatigue physiologically, behaviourally and psychologically and this assumption has led to the development of subjective and objective measurement tools. The assessment of fatigue self-report is the most direct way to access the dimensions of fatigue. More research is needed to answer important questions regarding the nature and dimensions of the fatigue experience. Most measures presently available have not demonstrated adequate reliability and validity in clinical populations. Measures should be selected with a comprehensive knowledge of the strengths and weaknesses of the instruments as well as in keeping with any conceptual model of fatigue. Fatigue can be defined from several theoretical perspectives, each of which may dictate specific measurement techniques. Within the field of fatigue associated with cancer, nurses are interested in clinical management and research applications of assessment tools. Information sources will therefore focus on a patients' subjective reports of their fatigue, and the impact of fatigue on functional ability and social functioning. Behavioural observation may have a role in fatigue management and may be of value as a method of establishing reliability of fatigue assessment by using multiple indicators of the fatigue construct.

It is well established that fatigue is a multidimensional experience. One immediate clinical and research implication of this multidimensional perspective is that fatigue assessment in health care settings must be multidisciplinary in nature. Capturing the multidisciplinary aspects of fatigue can mean measurement of basic biological processes - anatomy, physiology, neurophysiology and biochemistry. In clinical settings, fatigue assessment translates into assessments involving multiple biomedical specialities and extends to biobehavioural and psychosocial domains, invoking measurement of such

diverse dimensions as sensory, psychophysiology, cognition, affect, fatigue behaviour, and adoption of the sick role.

Piper's work discussed above is the most sophisticated attempt to capture the fatigue experience of patients. Others have field tested existing instruments, most notably the Pearson Byars Fatigue Feeling Checklist with clinical populations. For example, Cohen and Hardin (1989) provide estimates of the incidence and course of fatigue in people with botulism, Srivastava (1989) in patients with end-stage renal disease, and Jamar (1989) in patients receiving chemotherapy. This information gives us a perspective readily applicable to the care of these patients. We know that fatigue is a *bona fide* symptom of serious proportions in these patients and that interventions need to be designed to control or alleviate it. The material presented in this literature review represents our present ability to measure fatigue in clinical populations. The basis of fatigue may be quite different in healthy and sick populations and should be evaluated and measured with these differences in mind (Crosby, 1991). To further determine their clinical validity, the instruments need to be widely tested in subjects likely to experience fatigue. Concurrent testing with instruments to measure related phenomenon such as depression is needed to understand the divergence or convergence of these symptoms.

It is important to realise that previous research does not differentiate between the distinct components within the concept of fatigue. As stated above this is relevant to both measurement and methodological issues, but also in planning interventions to alleviate fatigue. Clearly future researchers needs to understand the mechanisms involved, whereby either physical or psychological influences affect the levels of an individual's fatigue. Interventions therefore need to be tailored in a way which interact with the relevant dimensions of this problematic symptom.

CHAPTER 4

FATIGUE AND THE CANCER EXPERIENCE

4.1 Cancer And Fatigue

This chapter reviews the research literature concerning fatigue in cancer patients, evaluating the quality of the evidence, thus helping to focus the direction and methodological rigour required in future investigations. Since fatigue in this population has been attributed to several mechanisms these will be discussed. The prevalence of fatigue in cancer patients will then be documented. An overview of what is currently understood about fatigue in cancer will follow. Based on the literature, conceptual and methodological difficulties will be described. Finally, gaps in understanding will be identified. Suggestions for future research will be formulated and potential interventions to decrease feelings of fatigue explored.

4.1.1 The basis of cancer fatigue

Fatigue is multifactorial and multidimensional; there are biological, psychological, social, and personal factors that possibly influence onset, impact, expression, duration, and severity of the fatigue experience. Most of the research on fatigue in cancer patients has not clearly identified specific correlates of fatigue. It is not clear how pre-existing conditions, direct effects of cancer, symptoms related to cancer, effects of cancer treatment, and the demands of dealing with cancer interact to produce or exacerbate fatigue. Research on other populations suggests some correlates that may be relevant for cancer patients. Possible correlates are reviewed below, because they represent areas that require further systematic investigation in cancer patients.

Little is known about the mechanisms of fatigue in cancer patients but the literature reviewed previously seems pertinent to the present discussion. The many different hypotheses about the causal mechanisms of fatigue referred to in Chapter 2 have not been adequately tested in a population of cancer patients. No experimental work has identified the physiological mechanisms that underlie the fatigue experience. A combination of mechanisms are likely. All are potentially relevant to explaining some

aspects of the fatigue experienced by the individual with cancer. Presently, the most reasonable approach to exploring the aetiology of fatigue in individuals with cancer is to consider multiple factors (Nail, 1990).

4.2.1.1 Cancer-orientated frameworks and models of fatigue

The broad categories of variables; personal characteristics, resource factors and illness characteristics proposed to affect fatigue in cancer patients have been reviewed. Vincent (1992) organised the multitude of factors according to the energy model of Ryden (1977). Ryden (1977) discussed energy balance as a critical consideration of the nursing process and provided a framework for incorporating psychosocial and physiological aspects of energetics, and depicts four variables that have impact on the energy capacity of the human system - energy sources, energy transformation, energy expenditure and energy response modifiers. The constant interaction and transaction among energy sources, transformation processes and expenditures lead to the development of an energy deficit for the individual with cancer. Such models are useful, allowing us to organise the multiplicity of factors associated with fatigue in cancer. The framework can be used to assess the possible causes in this specific patient group.

Aistair's (1987) framework based on energy and stress theory, implicates physiological, psychological, and situational stressors as contributing to fatigue. Reviewers have referred to this as a theoretical framework but Winningham, Nail, Barton Burke, Brophy, Cimprich, Jones, Pickard-Holley, Rhodes, St.Pierre, Beck, Glass, Mooney and Piper (1994), suggest it more accurately reflects a pretheoretical clarification of concepts.

Piper Lindsey and Dodd (1987) describe a framework for fatigue which permits the analysis of multiple discipline perspectives, definitions, and theories. Physiological, biochemical and psychosocial mechanisms most likely to influence fatigue symptoms are discussed. The framework holds a utility for researchers in terms of guiding assessment of potential aetiological factors related to fatigue. The application of theoretical frameworks addressing specific components of fatigue may enhance understanding of fatigue in patients with cancer. Such an example is the work of Cimprich (1992a, 1992b, 1993) who uses attentional theory to guide her research on attentional fatigue in women having surgery for breast cancer. A more general model such as that proposed in relationship to the morbidity of cancer patients by Thomas and Dodd (1992) could also be exploited within future study designs. The investigation of cancer-related fatigue currently is limited by a lack of well developed theoretical frameworks that can be used to guide clinically relevant research.

4.1.1.2 Somatic mechanisms

The following somatic mechanisms for fatigue have been proposed in patients with active disease or during treatment. Mechanisms most likely to influence fatigue in cancer patients include the liberation of intracellular products and metabolites resulting from cell lysis and necrosis of the tumour mass following chemotherapy and radiotherapy . It has recently been hypothesised that mechanisms may involve changes in skeletal muscle protein stores resulting from endogenous or treatment administered tumour necrosis factor (St.Pierre, Kasper and Lindsey, 1992). Fatigue may prove to be a manifestation of aberrations in energy availability and expenditure frequently encountered with cancer and its treatment, such as anorexia, cachexia and changes in metabolism (Kaemfer and Lindsey, 1986 ; Lindsey, 1986). Weight loss has been investigated in a sole study of patients receiving radiotherapy. Intuitive feelings were supported with empirical work; a positive association was revealed (Haylock and Hart, 1979). Further research is required to substantiate this relationship.

Alteration in the body's immune status (bone marrow depression possibly resulting in infection and fever) and ability to obtain and maintain oxygen levels induced by a state of anaemia or dyspnoea are frequently believed to induce fatigue (Maxwell, 1984). However, evidence for this link has not revealed consistent evidence. Fluid and electrolyte imbalance due to the disease (syndrome of inappropriate antidiuretic hormone secretion associated most notably with oat cell carcinoma of the lung, squamous cell carcinoma of the bronchus secreting parathyroid hormone, hypercalcaemia resulting from release of calcium from bone metastases) or treatment (diarrhoea and vomiting resulting in hypokalaemia, tumour lysis syndrome) could potentially affect neurotransmission (centrally and peripherally) and muscle force. This could result in fatigue and lethargy.

Insomnia is suggested to be a common occurrence in cancer patients (Kaye, Kaye and Madow, 1983 ; Silberfarb, Hauri, Oxman and Lash, 1985). No detailed investigation of the relationship between alterations in sleep and rest patterns and fatigue have been undertaken and the literature pertaining to sleep disturbance is contradictory (Beszterczey and Lipowski, 1977 ; Lamb, 1982).

The potential variation in the extent of fatigue and patterns according to aetiology and site are not documented in any detail. However, the finding that prevalence rates vary according to site or the particular phases of treatment lends support to the idea that treatment related factors may be important (Smets, Garssen, Schuster-Uitterhoeve and de

Haes, 1993). Nobody has addressed the issue of which somatic mechanisms might contribute to the persistent fatigue following successful cancer treatment, when symptoms of disease are no longer evident. It is probable that fatigue is due to a combination of mechanisms. Any differences in the dimensions of fatigue between patients with early and late stage cancer have not been systematically studied. Fatigue experienced during treatment is likely to be different in origin to that induced by the disease itself.

4.1.1.3 Symptoms

The constellation of symptoms, side-effects and medications used to control them may interact to produce fatigue. Fatigue does seem to be associated with pain (Blesch, Paice, Wickham *et al.*, 1991). Arathuzik (1991) in describing the pain experience of patients with metastatic breast cancer elicited fatigue as a common concern in relation to the pain experience. It also interfered with daily household and leisure activities. Lung cancer patients are acknowledged by clinicians as being constantly tired and this appears to be supported empirically. Brown, Carrieri, Janson-Bejerklie and Dodd (1986) related fatigue with the sensation of dyspnoea and it was suggested that dyspnoea may be construed synonymously with fatigue by patients with lung cancer.

Substantial evidence exists that cancer chemotherapy provokes substantial levels of emotional distress (Meyerowitz, Sparks and Spears, 1979 ; Burish and Lyles, 1983 ; Silberfarb, Holland, Anbar, Bahna, Maurer, Chahinian and Comis, 1983) and the processes that provoke distress have been elaborated by Leventhal, Easterling, Coons, Luchterland and Love (1986). In this team's research a major source of physical and emotional upset proved to be the combination of side-effects. Difficulty with treatment, disruption in social and work life and emotional distress and number of side-effects all correlated. The amount of distress generated was mediated by psychological processes such as interpretation of, and coping with, side-effects of treatment. Munkres, Oberst and Hughes (1992) more recently addressed the roles played by appraisal of the personal meaning of a situation and the resources available for dealing with it in directly mediating the effects of distress.

Leventhal and his co-workers (1986) suggested that some side-effects give rise to as much distress as the disease itself, because they are reminiscent of it, serving as strong reminders of cancer. The side-effect of tiredness might echo the disease because it accompanies most illnesses and might be confused with cancer. Limited support for this assumption was gained, because there was a greater likelihood for vague, long-term side-

effects such as tiredness to be associated with emotional distress. However, it was recognised that as tiredness can also be the result of emotional distress, it is plausible that such distress exacerbates or causes this state which the patient labels as a treatment effect. Temporal relationships between side-effect severity and distress remain unclear and should be explored in a longitudinal study to clarify causal relationships.

4.1.1.4 Psychological mechanisms

The above discussion supports the need to take into account the psychological component of fatigue. Emotional vulnerability has been observed by Weisman (1976) in newly diagnosed cancer patients and associated with fatigue. A variety of emotional responses and ineffective coping strategies are frequently reported in cancer patients (anxiety, depression, confusion, fear and anger). Such responses and the endurance of heavy stress over prolonged periods of time necessitating active coping associated with particularly distressing side-effects may contribute to fatigue (Nerenz, Leventhal and Love, 1982 ; Knobf, 1986 ; Blesch, Paice, Wickham *et al.*, 1991). The mental effort required to cope with the intense and competing demands imposed by a diagnosis of cancer may lead to attentional fatigue. Cimprich (1992a) has demonstrated a decline in the capacity for attention and concentration in women undergoing treatment for breast cancer in the initial phases of illness.

Collectively the evidence suggests that psychological distress is a potentially important variable to consider in studies of fatigue in cancer patients. Prolonged stress is proposed by Aistars (1987) as the main cause of fatigue in the person with cancer. Such responses may not only cause but also result in persistent fatigue. In cancer, depression and fatigue may co-exist, both resulting from identical biological factors (Hayes, 1991). More systematic studies need to be performed to investigate the relationship between depression, anxiety and the fatigue experience of cancer patients. The characteristics of the individual, including motivation, beliefs and attitudes and the individual's perception of cancer should be considered.

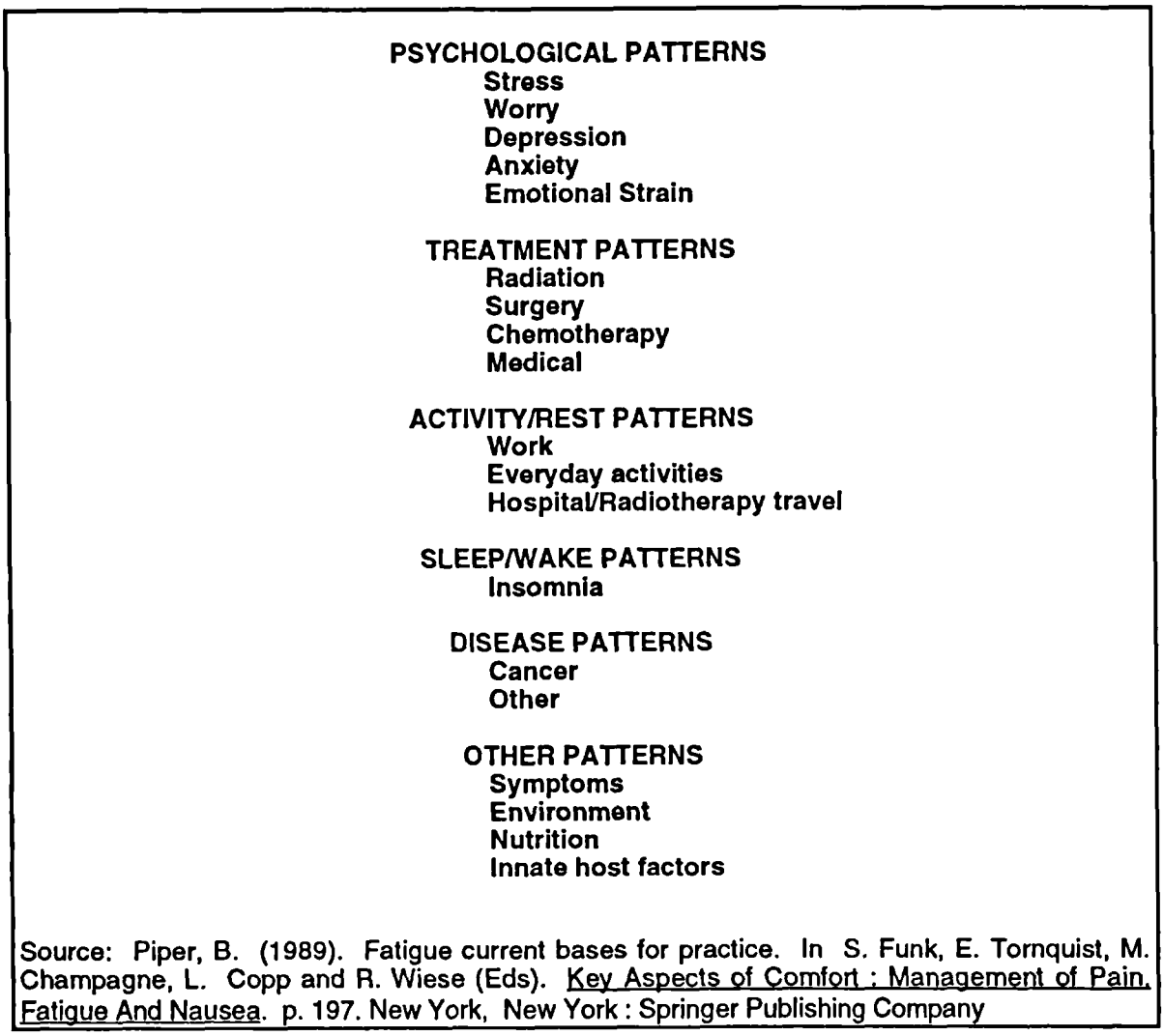
4.1.2.5 Social support

Resource related factors such as the perceived level of social support may be vital. It is important to understand the role social support plays in the perception and management of symptoms such as fatigue. The relationship between level of daily activities/functional ability and fatigue in individuals undergoing treatment for cancer has not been systematically evaluated. Thomas and Dodd (1992) developed a model for morbidity in ambulatory cancer patients, and of the indices selected to reflect the functional domain (functional status, social resources, economic resources, vigour and fatigue). Total function correlated with all the indices, although less so with vigour and fatigue. Both vigour and fatigue correlated with all the indices, except social resources. The results of this study should be viewed with caution as they are based on a secondary analysis of pre-existing data, and the instruments used in the original study may not have been ideally suited to measure the variables being studied in the construction of the model. Several studies have documented problems cancer patients experience in maintaining functional performance and have suggested a relationship between fatigue and disruption in functional performance status (Kubricht, 1984 ; King, Nail, Kreamer *et al.*, 1985 ; Rhodes, Watson and Hanson, 1988).

4.1.1.6 The patient's perspective

Our understanding of what accounts for fatigue in cancer patients has been supplemented by the opinions of the patients themselves. These have been documented by a number of researchers in small scale studies, for example, Pearce (1993) and McArthur (1992). Figure 4.1 summarises the perceived causes of fatigue in cancer patients documented by Piper (1989) in response to the question "What do you believe most directly contributes to or causes your fatigue?". We do not know how opinions vary over time, different stages in the disease and treatment trajectory Such information is vital as it will influence the selection of nursing strategies considered in the amelioration of fatigue.

Figure 4.1 Perceived causes of fatigue in cancer patients



Source: Piper, B. (1989). Fatigue current bases for practice. In S. Funk, E. Tornquist, M. Champagne, L. Copp and R. Wiese (Eds). Key Aspects of Comfort : Management of Pain, Fatigue And Nausea. p. 197. New York, New York : Springer Publishing Company

4.1.1.7 Coping responses to fatigue

Fatigue may appear unalterable to the patient, family and nurse, becoming synonymous with the challenge of living with cancer and its treatment. In living with fatigue patients develop many strategies and skills of their own over time. Much can be learned from studying the actual coping practices of patients who have long-term experiences of fatigue.

Strategies patients employ to deal with fatigue have been reported in the self-care research (Dodd, 1988a ; Dodd, 1988b ; Rhodes, Watson and Hanson, 1988 ; Nail, Jones, Greene, Schipper and Jensen, 1991 ; Robinson and Posner, 1992) and in some of the

descriptive and instrument development fatigue studies (Jamar, 1989 ; Piper, Lindsey, Dodd *et al.*, 1989). The self-initiated strategies most often selected by patients to deal with fatigue described in these studies have been summarised by Piper (1989) and appear in figure 4.2. What one patient finds useful may be of no benefit to another, although commonly recurring themes such as taking naps and resting, going to bed earlier and keeping busy to keep the mind off fatigue feature in the majority of the responses. However these are only partially effective in ameliorating the problem.

Figure 4.2 Patient initiated fatigue interventions

ACTIVITY/REST PATTERNS
- **Rest**
- **Nap**
- **Alter activities**
- **Sit/lie down**
- **Read**
- **Walk/exercise**

PSYCHOLOGICAL PATTERNS
- **Distraction**
- **Relaxation**

SLEEP/WAKE PATTERNS
- **Sleep**

OTHER PATTERNS
- **Nutritional**
- **Environmental**
- **Social**
- **Symptoms**

Source: Piper, B. (1989). Fatigue current bases for practice. In S. Funk, E. Tornquist, M. Champagne, L. Copp and R. Wiese (Eds.). Key Aspects of Comfort : Management of Pain, Fatigue And Nausea. p. 197. New York, New York : Springer Publishing Company

Robinson and Posner (1992) indicated that nurses and family members had little idea which interventions patients themselves indicated would be beneficial in reducing fatigue. A possible relationship between a patient's representation of fatigue and his/her selection of strategies has not been investigated. We should determine whether the coping strategies are developed from a patient's own experience or were learned from others. The previous research by Dodd (1988a; 1988b) reveals that health care professionals possibly play only a small part in this.

There is no differentiation in the current research between immediate strategies and long term alterations that are incorporated into the life-style. The experience of episodic fatigue versus persistent fatigue and other differences in the fatigue experience should result in researchers comparing and contrasting strategies used at differing stages

in the disease and treatment career of cancer patient. The efficacy of preventive versus reactive strategies should also be documented.

4.1.1.8 Interventions for fatigue

Some of our most common interventions are based on little or no empirical evidence for people with cancer. Results from earlier studies indicate that patients do not always expect fatigue to be a problem. Accurate and relevant preparatory information on the impending experience of what to expect in terms of fatigue during and following treatment could enhance the patient's ability to cope. Other studies have illustrated the practical value of such information in facilitating coping (Johnson and Leventhal, 1974), but we have little research to inform us of the incidence, time of onset, and duration of fatigue or efficacy of self-care activities routinely suggested to patients. Skalla and Lacasse (1992) have produced specific patient education material in relation to fatigue.

Drugs, exercise and rest studies have been summarised by Piper (1991a). Anecdotal and case studies are popular but she considers just eleven to be adequately designed. Samples vary from individuals with a primary complaint of fatigue who were adminstered doses of potassium or magnesium aspartic (Shaw, Chesney, Tullis, and Agersborg, 1962) to patients with a chronic pulmonary condition taking part in a rehabilitation programme including breathing and exercise programmes (Pardue, 1984). Amantidine therapy has been used in patients with multiple sclerosis (Murray, 1985) and the efficacy of rest evaluated in terms of its effect on raised intracranial pressure (Bruya, 1981). Gerber, Furst, Shulman, Smith, Thornton, Liang, Cullen, Stevens and Gilbert (1987) report the results of a prospective randomised pilot study comparing standard occupational therapy with a work-book based programme, designed to teach patients with rheumatoid arthritis energy conservation techniques. The results suggest that interrupting physical activity with rest periods may result in increased physical activity in this group of patients. Certain interventions may be helpful under certain circumstances and there is a need to test interventions which are realistic and relevant to cancer patients

In healthy individuals it is generally assumed that exercise is effective in reducing fatigue (Thayer, 1987). Exercise is often recommended as an integral component of cancer rehabilitation (Shaw, Chesney, Tullis and Agersborg, 1962 ; MacVicar and Winningham, 1986 ; Winningham and MacVicar, 1988 ; MacVicar, Winningham and Nickel, 1989 ; Winningham, MacVicar, Bondoc, Anderson and Minton, 1989 ; Winningham, 1991 ; Young-McCaughan and Sexton, 1991). So far this assumption has been supported by serendipitous findings and tested with breast cancer patients in

preliminary studies only. Results suggest that fatigue may be reduced by an exercise programme (Questad, Malec, Harvey, Kienker and Romsaas, 1982 ; Questad, 1983 ; Winningham, MacVicar and Johnson, 1985 ; MacVicar and Winningham, 1986 ; MacVicar, Winningham and Nickel, 1989 ; Young-McCaughan and Sexton, 1991) but this is subject to dispute (St.Pierre, Kasper and Lindsey, 1992).

Considering the hypothesised relationship of stress with fatigue in cancer patients, stress management resulting in a reduction of anxiety and promotion of coping are important outcomes that may decrease fatigue. Studies evaluating the effectiveness of psychotherapeutic interventions for cancer patients have found decreased fatigue scores to result (Spiegel, Bloom and Yalom, 1981 ; Forester, Kornfeld and Fleiss, 1985). Therefore, interventions aimed at reducing emotional distress or enhancing coping responses may be an effective way to decrease feelings of fatigue. Johnson, Nail, Lauver, King, and Keys's (1988) study with radiotherapy patients although not directed specifically at the symptom of fatigue suggest that the provision of information directed at preparing patients to view symptoms as a normal part of treatment rather than a sign of disease progression when appropriate may be beneficial. Diversional activity and its utility in enhancing coping has been explored by Radiewicz and Schneider (1992).

Unfortunately there seems little to recommend because at the present time fatigue interventions have not been adequately tested in cancer patients. The occurrence of fatigue across diagnostic and treatment categories, at all phases of the lifespan, underscores the need for empirically based interventions. The results of research studies infer a possible framework that might be useful. A multi-method fatigue therapy programme is likely to be the most effective and may include energy conservation activities, a planned exercise programme, stress reduction strategies and nutritional counselling. Interventions offered will need to be tailored to the needs of the individual patient.

4.1.2 Prevalence of cancer fatigue

Cancer and its treatment are characterised by a variety of possible symptoms such as pain, shortness of breath, nausea, loss of appetite and fatigue. Of these, investigators have found that patients report fatigue as the most disturbing symptom experienced during treatment (Rhodes, Watson and Hanson, 1988). It causes the greatest amount of interference with self-care (Fernsler, 1986). This has impact on such areas as ability to perform household tasks and enjoyment of leisure activities (Todres and Wojtuik, 1979),

This review of the literature was obtained by searching for studies in which fatigue was assessed or mentioned as part of a larger study usually where a symptom checklist was applied containing items concerned with fatigue, tiredness or loss of energy. Such a procedure does not lead to an exhaustive list of all studies which include fatigue as an outcome variable.

4.1.2.1 Chemotherapy

The prevalence of fatigue in cancer patients undergoing chemotherapy has been estimated. Coates, Fischer Dillinbeck, McNeil, Kaye, Sims, Fox, Woods, Milton, Solomons and Tattershall (1983) surveyed a varied group of chemotherapy patients asking them to identify and rank physical and non-physical side-effects. Experiencing constant tiredness was ranked highly overall, but its relative importance to other symptoms varied on a number of factors. Meyerowitz, Sparks and Spears (1979), whilst outlining the psycho-social implications of adjuvant chemotherapy in breast cancer patients, reported fatigue in 96% of the sample (n=50). It was heralded as the most common and disruptive symptom. Frequent and dramatic changes in activity levels were often the result, a finding supported by Frank-Stromborg and Wright (1984). Studies involving patients receiving chemotherapy for a variety of different types of cancer report incidence ranging from 59% to 82% (Nerenz, Leventhal and Love, 1982 ; Cassileth, Lusk, Bodenheimer, Farber, Jochimsen and Morrin-Taylor, 1985 ; Nail and King, 1987 ; Nail, Jones, Greene *et al.*, 1991). Fatigue has also been identified to be the most *distressing* side-effect reported by patients receiving chemotherapy (Knobf, 1986 ; Strauman, 1986). The predominance of fatigue in cancer patients treated with chemotherapy is also supported through non-statistical descriptive accounts and clinical observations (Fernsler, 1986 ; Rhodes, Watson and Hanson, 1988).

Cassileth, Lusk, Bodenheimer *et al.'s* (1985) study illustrated that patients about to receive chemotherapy consistently underestimated the possibility that they would experience side-effects including feeling tired. The frequency of expected side-effects was much greater than patients anticipated. Tiredness was one of the most common reported side-effects. Patients' expectations failed to predict their occurrence or severity.

Related to this, Teirney, Taylor and Jose Closs (1989) in a detailed descriptive study of breast cancer patients receiving chemotherapy, revealed discrepancies between the side-effects that patients had expected would be most difficult to cope with and those that they actually found in reality to be the most problematic. The focus of the study was alopecia. However, a considerable amount of data were collected on other aspects.

Tiredness was singled out as the most often reported side-effect. It was reported by 87.5% of the sample (n=60) at any stage of treatment, generating a great deal of comment and concern among patients. Only a couple of women had expected tiredness to be so frequent or so problematic to cope with, and only half had been forewarned. It appeared to become more problematic as treatment progressed, but interestingly in this study, it was one of the few side-effects perceived to be under the patient's control.

In a substantial group of both cross-sectional and longitudinal studies factors contributing to emotional distress in lymphoma and breast cancer patients receiving chemotherapy on an adjuvant basis or for metastatic disease were outlined. Analysis was based on an explicit theoretical view of patient adjustment to treatment (Leventhal, Meyer and Nerenz, 1980 ; Leventhal and Johnson, 1983 ; Nerenz and Leventhal, 1983 ; Leventhal, 1990) . A number of parallel studies were performed (Nerenz, Leventhal and Love, 1982 ; Ringler, 1983 ; Leventhal, Easterling, Coons *et al.*, 1986 ; Love, Leventhal, Easterling and Nerenz, 1989). Patients reported side-effects of treatment and their efforts to control them, their knowledge and beliefs about their illness, strategies for monitoring the effectiveness of treatment and the extent to which they had been prepared for their experiences of chemotherapy. Only 12% anticipated tiredness. However, 89% experienced tiredness sometime during the first six cycles. It frequently defied successful coping attempts, possibly exacerbating feelings of failure to control the side-effects and represented a source of upset.

4.1.2.2 Radiotherapy

There is substantial evidence to suggest that fatigue is also an important clinical problem for patients undergoing radiotherapy. The reported incidence of fatigue as a side-effect in studies where patients receive external or intracavity radiation has been documented, ranging from 65% to 100% (Peck and Boland, 1977 ; Kubricht, 1984 ; King, Nail, Kreamer *et al.*, 1985 ; Oberst, Hughes, Chang and McCubbin, 1991 ; Nail, 1993). Fatigue appears to peak and wane over the course of treatment (Greenberg, Sawicka, Eisenthal and Ross, 1992). Among subjects receiving radiotherapy to specific anatomic sites, interviewed weekly during the course and once a month for three months after the completion, the highest incidence of fatigue was found in patients receiving radiotherapy to the chest (King, Nail, Kreamer *et al.*, 1985).

4.1.2.3 Biological therapy

In a review of the use of interferon, fatigue was reported to be the most prevalent symptom, the most important dose-limiting toxic effect, and the most difficult side-effect to manage (Quesada, Talpaz and Rios, 1986). Anecdotally information seems to indicate fatigue is more severe in this group of patients than in those receiving any other treatment modality such as chemotherapy or radiotherapy. It has been consistently documented that patients receiving biotherapy (interferon, interleukins, colony-stimulating factors and tumour necrosis factor) experience fatigue as a significant, and at times dose limiting side-effect, although information is limited about fatigue patterns in the biotherapy literature. Piper, Reiger, Brophy, Haebur, Hood and Lyver (1989) synthesised what is currently known on this, based mainly on clinical observation and unpublished data.

4.1.2.4 Surgery

With the exception of Cimprich's (e.g. 1993) work, studies of surgical patient fatigue do not involve patients with cancer. Though not specific to cancer patients, an abundance of evidence documenting the occurrence of fatigue after surgery has been presented in a review by Rhoten (1982). The adjustment to low energy levels required of patients and their families on return home has been confirmed by Oberst and James (1985). Fatigue after surgery is particularly relevant to cancer patients who receive adjuvant therapy because they have often not recovered prior to further treatment commencing. The possible cumulative effects of sequential treatments may increase the risk for the occurrence of fatigue in such a population.

4.1.2.5 Following treatment

Evidence that fatigue continues after radiotherapy and chemotherapy treatment protocols have been completed is limited (Eardley, 1986 ; Fobair, Hoppe, Bloom, Cox, Varghese and Spiegle, 1986 ; Knobf, 1986 ; Devlen, Maguire, Phillips, Crowther and Chambers, 1987 ; Bloom, Gorsky, Fobair, Hoppe, Cox, Varghese and Spiegel, 1990 ; Berglund, Bolund, Fornanader, Rutqvist and Sjoden, 1991) and has been the sole focus of only one small project (McArthur, 1992). Fatigue remained a significant problem for many months. An interest in this time period in the *survivorship* and *rehabilitation* literature may reveal more detailed accounts of the influence of fatigue on these patients' lives. We probably underestimate the residual effects of therapy. Comparison to a healthy control population is needed and identification of predictive factors sought in those most likely to be affected by low levels of energy.

Individuals or family members serving as primary caregivers for a person with cancer are recognised as at risk (Jensen and Given, 1991). An understanding of the factors leading to fatigue in such people can contribute to support of both the patient and caregiver.

4.1.2.6 Advanced cancer

In advanced cancer the literature refers to the term *asthenia* . This is considered a clinical syndrome characterised by generalised weakness as well as mental and physical fatigue (Bruera, Carraro. and Roca, 1984 ; Bruera, Roca and Cedaro, 1985 ; Bruera, Brenneis, Michaud, Rafter, Magnan, Tennant, Hanson, Tennant and MacDonald, 1989). Bruera has summarised the limited literature available. Two different symptoms are usually subsumed under the term : "(A) fatigue or lassitude, defined as easy tiring and decreased capacity to maintain adequate performance and (B) generalised weakness, defined as the anticipatory subjective sensation of difficulty in initiating a certain activity, this does not include the localised or regional weakness resulting from neurological or muscle disorders" (Bruera and MacDonald, 1988, p.9). Work on the experience of symptom distress has begun with this specific population (Sutcliffe, 1993) and will contribute to the knowledge base in this area. The perceived inevitability of fatigue up until now has encouraged a negative or neutral approach to its management.

4.1.2.7 Summary

Many patients with cancer have identified fatigue as a frequent and significant symptom. To date there have been few studies to systematically register the number of cancer patients experiencing fatigue which also take into account the stage of the disease process and the extent of the problem. Most studies reporting the incidence of fatigue as a side-effect of cancer treatments have limitations in that they include subjects presently under treatment as well as those who have completed treatment, subjects are interviewed only once so it is impossible to establish any pattern and patients with a variety of tumours, treatments, sites of treatments and stages of disease are included. In spite of these limitations it can be concluded that there is strong evidence to suggest that fatigue is a prevalent problem among patients receiving treatment for cancer and probably varies according to the phase and time of treatment (Haylock and Hart, 1979 ; de Haes, Raategever, Van der Berg, Hamersma and Neijt, 1987). Research to determine whether the fatigue produced by sequential or combined modality treatment exceeds that produced

by a sole treatment is needed to predict the responses of patients who receive multiple forms of cancer treatment. Measurement is a consistent problem. In the forgoing studies, single items were used to assess fatigue and typically fatigue is measured as a single criterion of symptom distress. This limited approach does not consider the multidimensional features of fatigue. Studies specifically addressing fatigue in this patient group will now be addressed.

4.1.3 Present state of knowledge of fatigue in cancer patients

This section appraises the research literature directly concerned with fatigue in cancer patients (see tables 4.1-4.4) because their cumulative findings are of direct value to nursing practice. Irvine, Vincent, Bubela, Thompson and Graydon (1991) and Potempa (1993) have previously critically appraised the research literature on fatigue in the individual with cancer. However, they fail to differentiate in their review between studies which focus on fatigue as the main variable of the study and those in which it is not the main focus of the research.

4.1.3.1 Nature of studies

Studies investigating fatigue in cancer patients have been restricted primarily to those patients undergoing treatment with chemotherapy or radiotherapy. Less is known about the correlates of fatigue or the occurrence of fatigue in cancer patients before and after treatment. Research studies to explore the topic explicitly may be categorised as follows;

- Those describing fatigue in a specific group of cancer patients e.g. Davis (1984) and Jamar (1989)

- Comparative studies describing different groups of cancer patients, the independent variable being the type of treatment e.g. Blesch, Paice, Wickham *et al.* (1991) and Haylock and Hart (1979)

- Studies comparing cancer patients to non-cancer patients ; either patients with other diseases or healthy individuals e.g. Pickard-Holley (1991).

A primary question often posed by practitioners is "Does fatigue differ in these groups ?". From the studies conducted to date we are unable to conclude that differences between groups of cancer patients are primarily related to certain factors. It is commonly assumed

that cancer and cancer treatment has a severe and negative effect on fatigue. Support for the assumption that fatigue is worse in this population than in others is lacking. To test this hypothesis comparative studies need to be performed with cancer patients and healthy controls. Marked differences between groups will only be uncovered if objective, sensitive indicators are utilised. With only one exception (Pickard-Holley, 1991) the studies have not included a comparison group permitting fatigue in cancer patients to be compared with other populations. This particular study failed to demonstrate any difference between a small number of cancer patients and a healthy control group. Findings such as these may be due to the operationalisation of the concept, methodological aspects of the study or psychological mechanisms that have influenced fatigue but which have not been taken into account. McCorkle and Benoliel (1983) found in a study concerned with symptom distress that patients with lung cancer were less vigorous and more fatigued than patients who had had a myocardial infarction. It is unclear whether the lung cancer sample were undergoing chemotherapy at the time of data collection.

4.1.3.2 Defining and operationalising the concept of fatigue

The meaning attributed to the concept of fatigue is rarely made clear, nor how the definition has been interpreted within a particular study. A number of terms may be used interchangeably. Fatigue is often operationalised as the subjective feeling of tiredness and lack of physical energy. Fatigue is considered to be a multidimensional construct but this is not always reflected in the choice of measurement strategies. Researchers also assume that certain spheres of life are affected by fatigue. As a clear framework is lacking and the dimensions of fatigue that should be considered unclear, the choice of areas is based on intuition. Authors generally include the presence of other symptoms, psychological well being and the performance of activities. Social functioning or social support may account for unexplained variance. Material areas such as the impact of fatigue on economic welfare should not be neglected. Choice of areas and operationalisation of the concept is not consistent and this creates difficulties in making comparisons.

Table 4.1 Summary of cancer nursing research concerned with fatigue in radiotherapy patients

Study Ref.	Sample & Aims	Study Design	Instruments	Main Findings
Haylock & Hart (1979) Fatigue in patients receiving localised radiation	In-patients and out-patients with cancer at various sites n=30 The major questions of the study were; 1.Does localised RT precipitate a fatigue which exhibits a pattern of intensity related to the duration of treatment ? 2.Does localised RT precipitate a state of fatigue which is charact-erised by a specific constellation of symptoms ?	Descriptive/correlational & comparative Prospective (each day of radiotherapy [RT])	Fatigue Symptom Checklist (FSC) Pearson Byars Fatigue Feeling Checklist (PBFFC)	There was a consistent drop in fatigue scores on sundays throughout the study. Lung and breast cancer patients experienced a significant change in baseline fatigue to the highest fatigue score reached (p < .068). Time since surgery was significantly related to mean fatigue levels (r = .34, p< .07). Weight was negatively correlated with fatigue (r = - .54, p < .002). Subjects who underwent the most lengthy regimes had the greatest change in fatigue levels. On the FSCL the symptoms tired in whole body, tired legs, heavy head, wanting to lie down & feeling ill correlated with fatigue levels experienced.
Kobashi-Schoot, Hanewald, Van Dam & Bruning (1985) Assessment of malaise in cancer patients treated with radiotherapy	Cancer patients receiving out-patient RT n=95 To develop a quantitative approach to assess malaise.	Descriptive/correlational & comparative Prospective (Each Monday and Friday over 3 weeks)	Questionnaire ; A) Fatigue Symptom Checklist (FSC) B) Checklist For Cancer Patients (CCP) C) Malaise Scale - 4 visual analogue scales D) Ill-well dimension scale E) Questions on hours of rest during the day and daily activities	Physical fatigue corrlated highest with the no. of hours rest during the day (r= 0.58, p < .001). Ill-well dimension correlated with malaise (r = .74, p < .001). ANOVA revealed there was a significant increase in physical fatigue and malaise over the course of RT. Patients with lymphoma and uterine cancer suffured less following a weekend, this was not observed for breast and bladder patients. There was no change in emotional state and no correlation of any of the variables measured with age.
Piper, Lindsey, Dodd, Ferketich, Paul & Weller (1989) The development of an instrument to measure the subjective dimension of fatigue	Breast or lung cancer out-patients receiving RT n=50 1. To explore the initial psychometric properties of an instrument constructed to measure multiple dimensions of fatigue. 2. To describe the baseline patterns of fatigue experienced by radiation therapy patients using the above tool	Descriptive/correlational Retrospective	Piper Fatigue Scale-Baseline (PFS-B) Profile Of Mood States (POMS) Fatigue Symptom Checklist (FSC)	Moderate evidence for discriminant and convergent validity of the PFS was found. The majority of patients had experienced an increase in fatigue score (PFS) during the 6 months before diagnosis, but most patients reported their fatigue as mild, intermittent and acute. Most patients believed that illness was the cause of their fatigue. Sleep and lying down for short periods were reported as effective in relieving fatigue. The average no. of FSC symptoms reported was 6.36. Stage of disease did not affect the number, type, or intensity of fatigue symptoms significantly. Lung cancer patients tended to start RT at a higher level of fatigue than breast cancer patients.

Table 4.2 Summary of cancer nursing research concerned with fatigue in chemotherapy patients

Study Ref.	Sample & Aims	Study Design	Instruments	Main Findings
Rhodes, Watson & Hanson (1988) Patients' descriptions of the influence of tiredness and weakness on self-care abilities	Cancer patients who have received 6 pulses of chemotherapy (CT) $n = 20$ To examine retrospectively, utilising an interview schedule, the relationship between patients' self-reported symptoms and their self-care activites during anti-neoplastic chemotherapy, and to describe these findings within the Self-Care Defecit Theory of Nursing.	Descriptive Retrospective	Self-care telephone interview schedules A and B A) Regarding self-care and symptoms B) Regarding self-care and fatigue	Tiredness and weakness were identified as the symptoms that most interfere with self-care activities in interview A. 9 out of 11 subjects identified self-care activities on the day of CT and day following CT as limiting the expenditure of energy. These were categorised into limiting the expenditure of energy by planning/scheduling activities, decreasing non-essential activities, and increasing dependence on others for home management, transport and care dependence
Pickard-Holley (1991) Fatigue in cancer patients - a descriptive study	Ovarian cancer patients (stage IIB - IIIC) receiving CT $n=12$ Healthy female controls $n=12$ To examine whether there were any relationships between fatigue, and various physical and psychological factors in women undergoing treatment for cancer	Descriptive/correlational & comparative Prospective (day 1, 7, 14 & 21) and cross sectional (varying pulses of CT)	Rhoten Fatigue Scale (RFS) Beck depesssion Inventory (BDI) Gynaecology Oncology Group Performance Scale Karnofsky Performance Scale CA125 weight change and other lab values	Weak to moderate relationships found between levels of fatigue and CA125 levels. As CA125 levels decrease fatigue also decreases. There was no significant difference between the mean fatigue score of the patient and control group. The fatigue trajectory was found to peak at day 7 and slowly decline during the remainder of the 28-day cycle. No significant relationship was found between fatigue and age, stage of disease, course of treatment or depression.
McArthur (1992) A study of fatigue in cancer patients receiving chemotherapy	$n=35$ Group A receiving CT $n=17$ Group B completed CT attending out-patients $n=18$ 1. To examine the extent of the problem of fatigue in a cancer population. 2. To determine what effect chemotherapy has on the individual's level of fatigue 3. To identify perceived causes of fatigue and relief measures. 4. To develop a conceptual framework which may be used to provide effective nursing interventions.	Descriptive/correlational & comparative Prospective Group A prior to 1st CT, at nadir and prior to 2nd CT Cross-sectional Group B on one occasion	Piper Fatigue Scale (PFS)	94% of group A had some degree of fatigue, and 50% in group B. No statistical evidence to suggest any significant difference between the mean fatigue scores of group A prior to CT and Group B. No statistical difference in fatigue scores between ovarian and non-ovarian patients. Statistically significant increases in affective and severity dimensions in Group A fatigue scores over time.
Jamar (1989) Fatigue in women receiving chemotherapy for ovarian cancer	Women receiving out-patient CT For ovarian cancer (stage I - IV) $n=16$ The puposes of the study were to obtain descriptions of the phenomenon of fatigue in individuals receiving chemotherapy, to determine if there is an identifiable fatigue pattern related to the chemotherapy cycle, and to determine the effect of fatigue on activity level and lifestyle on the individual.	Descriptive/correlational Cross-sectional	Semi-structured interview including items on sleep pattern, activity level, accounts of the fatigue experience and strategies used to relieve fatigue Profile Of Mood States-Short Form (POMS-SF) Symptom Distress Scale (SDS) Pearson Byars Fatigue Feelling Checklist (PBFFC)	A pattern of fatigue related to the chemotherapy cycle emerged, worse in the first week following CT lessening prior to next pulse of CT. Symptom distress was related to increaes levels of subjective fatigue. Physical descriptors, emotional descriptors and descriptors related to changes in energy level were used to decribe fatigue. Levels of fatigue were significantly related to living arrangements, single parents and women without assisstance at home generally had higher levels of fatigue.The PBFFS significantly correlated with total SDS ($r = .6249$, $p < .001$) and with nauses and fatigue subscales ($r = 0.5811$, $p < .01$, $r = .8656$, $p < .001$) and the POMS-SF total score ($r = .6405$, $p < .01$).

Table 4.3 Summary of cancer nursing research concerned with fatigue in biological therapy patients

Study Ref.	Sample & Aims	Study Design	Instruments	Main Findings
Davis (1984) Interferon-induced fatigue	Malignant Melanoma patients receiving Interferon-alpha 2 I.V daily for 4 weeks *n*=16 To identify the degree of fatigue experienced and the impact on functionability of patients with malignant melanoma receiving interferon-alpha 2.	Descriptive/correlational Prospective (Days 0, 12 and 26)	Pearson Byars fatigue Feeling Checklist (PBFFC) Fatigue Symptom Checklist (FSC) Sickness Impact Profile (SIP)	Significant correlations were found between the cumulative dose of IFN, the fatigue scores, and no. of fatigue symptoms. Significant negative changes occurred in sleeping, eating, mobility and social activity patterns. Most frequently reported physical symptoms of fatigue were leg weakness and a need to lie down, while difficulty thinking and impatience with others were frequent mental symptoms.
Rieger (1987) Interferon-induced fatigue : a study of fatigue measurement	Cancer patients receiving Interferon alpha and gamma by variable route and dose *n*=30 To describe changes in fatigue, functional status , and muscular strength as experienced by cancer patients receiving interferon therapy	Descriptive/correlational Prospective (Pre therapy, one week and one month post therapy	Pearson Byars Fatigue Feeling Checklist (PBFFC) Functional Living Index - Cancer (FLIC) Jamar Hand Held Dynamometer	No significant differences were found over time in subjective fatigue, functional status and muscular strength. Significant negative correlations were found between the PBFFC and the FLIC.
Robinson & Posner (1992) Patterns of self-care needs and interventions related to biologic response modifier therapy : Fatigue as a model	Cancer patients who have had at least one treatment receiving Interferon - alpha, Tumor Necrosis Factor or Interleukin-2 and a designated family member and nurse *n*=16 patients The objectives of the study were : 1. To conduct a pilot study of the High-Intensity Self-Care needs and Interventions survey 2. To describe the patterns of self-care needs and interventions among patients receiiiving inpatient or outpatient biotherapy	Comparative Cross-sectional	Analysis Of High Intensity Self-Care Needs And interventions Survey	Patient and family members responses correlated well. In several parameters including degree and duration of fatigue nurses' perceptions did not correlate at all with patients. There was minimal agreement among patients, family members and nurses responses as to the interventions that could be used by others to help patients cope with fatigue. It was considered that the instrument should be shortened and questions clarified.

Table 4.4 Summary of cancer nursing research concerned with fatigue in radiotherapy and chemotherapy patients

Study Ref.	Sample & Aims	Study Design	Instruments	Main Findings
Blesch, Paice, Wickham, Harte, Schooner, Purl, et al. (1991) Correlates of fatigue in people with breast or lung cancer	n=77 Lung cancer patients (n=33) and breast cancer patients (n= 44) receiving CT and/or RT as in or outpatients The study aimed to: 1. Discern behavioral, physiological, and biochemical factors that may be linked with subjective ratings of fatigue reported by adults. undergoing active treatment 2. Examine the psychometric properties of three instruments used to measure fatigue.	Descriptive/correlational Cross-sectional	Rhoten Fatigue Scale (RFS) and Checklist (ROC) Profile Of Mood States-Short Form (POMS-SF) Medical record audit for values of biochemical and physiological correlates of fatigue Questionnaire on pain, sleep and social support	Fatigue was present in 99% of sample ; 64% rated fatigue as moderate to severe. Significant correlates of fatigue intensity were pain severity (r = 0.48, p < .0001), total mood disturbance (r = .48, p < .0001) and several subscale scores of POMS-SF. Mean fatigue levels between breast and lung patients were not significantly different. Fatigue did not correlate with any biochemical parameters and only one physiological correlate, pain. Duration of illness positively correlated with fatigue in breast patients, but not in lung patients. The ROC data was found to be very inconsistent and therefore not used.
Piper, Ok Lee, Kim, Pak & Kim (1990) Fatigue - transcultural implications for nursing practice	American and South Korean Breast cancer patients receiving RT or CT n=74 (American) n=11 (Korean) 1. To investigate fatigue patterns and self-initiated interventions in Korean women with breast cancer. 2. Compare findings to fatigue patterns and interventions documented in North American women with breast cancer.	Descriptive/correlational & comparative Prospective (first 3 weeks of RT and weekly during first 2 pulses of CT)	Profile Of Mood States (POMS) Piper Fatigue Scale (PFS) (Times 1-3, weekly) Korean women Hae Ok Lee Checklist (HOFC) (Times 1-3, weekly)	Average total fatigue score of patients (30.5) on HOFC slightly lower than average fatigue scores of healthy workers in a previous study. No change over time in POMS for RT patients or for Korean women receiving CT. RMANOVA revealed American women receiving CT total mood disturbance scores were significantly greater on day 1 of 2nd pulse of CT (F , 10.49 ; p< .0001), and significantly less vigor was reported (F , 10.750 ; p < .0001). Total fatigue scores on the PFS did not vary between two groups or by treatemnt. Fatigue scores did not appear to change over time in the Korean sample; in the American sample in women receiving CT, the mean sensory scores and total fatigue scores changed significantly over time.

4.1.3.4 Subjects and methods

Three studies of radiotherapy patients have consistently found that the prevalence of fatigue increases over the course of radiotherapy (Haylock and Hart, 1979 ; Kobashi-Schoot, Hanewald, Van Dam *et al.*, 1985 ; Piper, Lindsey, Dodd *et al.*, 1989). The pattern varies, occurring intermittently at the start and becoming continuous as treatment progresses. More is known about the prevalence, duration and pattern of fatigue in patients receiving radiotherapy than other treatment groups (Irvine, Vincent, Bubela *et al.*, 1991). Four studies have been conducted with a sample of patients receiving chemotherapy. A decline in fatigue scores is generally recorded after drug administration has concluded.

Differences in methodology and treatments preclude meaningful comparisons, although it may be concluded that fatigue is troublesome. Contributing to a lack of knowledge are a number of measurement issues. Four groups of studies are distinguished. Firstly, some authors developed *ad hoc* questions to measure fatigue and fail to report validity and reliability of the instruments used. A second group of investigators used measures developed in other fields to study fatigue in cancer patients. These scales refer to psychological adjustment and functional status such as Profile Of Mood States and the Sickness Impact Profile. Measures used to study fatigue in other populations such as industrial workers comprise a third group (the Fatigue Symptom Checklist and Pearson Byars Fatigue Feeling Checklist). In a fourth type of study, specific instruments have been developed to measure fatigue in cancer patients (the Piper Fatigue Scale). Some reliability and validity testing has been performed for most of these instruments in the latter three groups, but is limited. The advantages and disadvantages of various self-report methods need to be explored in some detail with consideration to what constitutes the best time to measure fatigue in cancer patients.

Studies cover a wide range of patient groups but samples are small and differ along medical dimensions : the type of tumour, the stage of disease, the treatment received, and in the differing points in treatment. Small sample size makes it difficult to discern genuine differences. A second issue relates to the control of background variables. Medical parameters are assumed to be the independent variables influencing the fatigue of cancer patients. Only in a few investigations have the groups been compared with respect to such variables as age, sex and time elapsed since treatment. These may explain a substantial part of the variance of the dependent variable fatigue.

Thus research methods do not seem altogether adequate in many of the reviewed studies. Some have small sample sizes, many do not consider intervening variables, and the instruments used have not always proved reliable and valid. The design of studies has not always been sufficiently rigorous. Interest is continuing to be generated as a number of abstracts have appeared in international conference proceedings (Piper, Ok Lee, Kim *et al.*, 1990 ; de Meyer, 1991 ; Piper, 1991b ; Piper and Dodd, 1991 ; Barrere, Trotta and Foster, 1993 ; Berger, 1993 ; Piper, Lindsey, Dodd, Ferketich, MacVicar and Paul, 1993 ; Yeager, Dibble and Dodd, 1993) but this method of reporting allows limited reflection on the methods utilised and how these may influence findings.

4.1.3.5 Theoretical notes

Strategies to develop nursing theory related to fatigue need to be identified. These could be used to guide research and practice. The ultimate goal of such theories will be to identify and predict which patients are at high risk of developing fatigue in order to test specific nursing interventions that prevent or ameliorate its occurrence.

Piper, Lindsey and Dodd's (1987) framework takes a deductive approach derived from the five disciplines which have investigated fatigue (psychology, physiology, ergonomics, medicine and nursing). This framework often forms the theoretical base of current studies, and is used to guide the selection of variables for study and the structure of the data collection instruments (for example Blesch, Paice, Wickham *et al.* 1991). Additionally conceptual frameworks developed for nursing have underpinned a number of studies, such as Orem's Theory of Self-Care and Levine's Conservation Model. Concepts derived from these frameworks have been related to the research questions or used as the organising framework for the study, for example the studies of Piper and Dodd (1991) and de Meyer (1991). The inductive approach to theory development in this area tends to have been ignored or weighted in favour of the deductive approach and the domains of fatigue open to study justified theoretically.

It is assumed that some cancer treatments are more likely to culminate in fatigue than others and that the fatigue of cancer patients is worse than that of the normal population. It is possible that cancer and cancer treatment influence fatigue less than is generally expected. However, if we agree that fatigue is a subjective evaluation of the patient, theoretical arguments can be raised to explain why such a seemingly disruptive disease as cancer does not consistently lead to a heightened evaluation of fatigue. One explanation may be provided by reference to Helson and Bevan's (1967) adaptation level theory. They formulated the theory to determine what conditions lead to a judgement of

neutral with a verbal rating scale technique. In their view, adaptation of a person at any given time is a weighted geometric mean of all stimuli, past and present, and the effects on the attribute being judged. The adaptation level changes when new stimuli are experienced. The neutral judgement corresponds to this adaptation level, and all other judgements are made relative to this. If cancer patients are asked to judge their fatigue, their judgement may be based on an adaptation level influenced by the experience of disease. As cancer patients may have experienced more extreme negative stimuli, their neutral point may refer to a more negative objective situation. Thus similar circumstances may lead to a more positive judgement of cancer patients than of healthy individuals. This mechanism creates methodological problems. The score given on a scale may have different meaning for cancer patients.

Breetvelt and Van Dam (1991) employ the term *response shift* to refer to the change in a person's internal standard for determining his or her level of functioning on a given dimension. The experience of fatigue during radiotherapy or chemotherapy, could change a patient's criteria for measuring fatigue. What had been perceived as *intense fatigue* before treatment, might be labelled *slightly fatigued* after having experienced exhaustion during treatment. The possibility of response shift complicates the interpretation of comparison data. One strategy suggested by these authors may be to ask subjects to rate pre-treatment ratings of fatigue at the same time as post-treatment scores as such scores will be assigned from the same perspective and therefore free from response shift bias. Further research is required to refine techniques for the assessment of response shift with regard to symptom reporting.

4.1.4 Summary and future research directions

Studies of fatigue in cancer patients and other populations have been reviewed. Looking at the research carefully it becomes evident that knowledge is insubstantial. A factor contributing to the lack of knowledge is a paucity of nursing studies that address fatigue in cancer patients. In the past fifteen years only eleven nursing studies have been published in sufficient detail to allow critique that address fatigue as their primary focus. Three main areas must be addressed if our understanding of fatigue is to advance in a clinically relevant manner.

First, it is imperative that we develop valid and reliable ways of measuring the presence and intensity of fatigue. Research to date has many design and measurement problems. Typically studies fail to include a control group, do not control for confounding variables, and have restricted measurement to unidimensional scales with

limited reliability and validity. For instance, many of the studies have employed a cross-sectional design with no control group. Consequently there is no reliable way of ascertaining whether fatigue is any different for cancer patients than for healthy individuals, or for patients undergoing treatment versus those who are not. With few exceptions most studies have failed to acquire an inception cohort of subjects. Studies employing a prospective design such as that by Pickard Holley (1991) are lacking. Lack of an inception cohort precludes controlling the lapse of time since diagnosis or treatment. Patients should be identified at an early and uniform stage so that the clinical course of fatigue can be clearly identified.

Most studies are concerned with patients receiving treatment, there is an absence of studies following the completion of therapy. Many are constrained by the cross-sectional approach. Cross-sectional study designs, in addition to heterogeneous samples of patients with a variety of tumour types, extents of disease, wide age range, and varying treatment, introduce constraints under which research findings must be viewed as tentative. The number of patients involved in these studies is often small, limited to cancers of the breast, ovary, lung and the lymphomas. Future challenges lie in employing comparative and longitudinal prospective design to reveal patterns and implications of fatigue for the individual concerned and their family.

The measures used to evaluate fatigue have often been unidimensional and non-standardised, with limited validity and reliability testing. Issues related to instrument development have been outlined in a previous chapter. Fatigue has mostly been assessed by single items in general symptom checklists or mood rating scales. There are few specific instruments used in the cancer patient population. Here measures of fatigue are incorporated into instruments intended to measure broader aspects of patient functioning. A more comprehensive instrument, thoroughly tested for its psychometric properties, is not yet available.

Secondly, we must describe patient characteristics associated with fatigue. While several correlates have been postulated, research to date has failed to verify consistent relationships between fatigue and other factors such as sleep disturbance, weight loss and psychological distress. Further work is needed between these and other correlates of fatigue. While there is evidence to suggest that fatigue interferes with the cancer patient's functional performance status, much of this work has been based on quantitative assessments with limited reliability and validity. It could be strengthened by the use of valid and reliable standardised scales measuring functional status. The outcome of fatigue has not been studied. Impact on quality of life, mobility, self-care, social

isolation, role change and family and caregiver fatigue, negative treatment and disease outcomes need to be explored in more detail.

Researchers and practitioners need to determine those interventions effective in reducing or eliminating fatigue. Studies are particularly needed in those areas where nursing could affect patient outcomes, and that are specific to different populations and situational contexts.

The research emphasis has undoubtedly focused on quantitative issues in the last two decades. We also need to document the fatigue experience from the patient's perspective. A broader view of a person's response to fatigue rather than the often narrow focus found in other disciplines should now be reflected in the research conducted. In-depth interviews of the fatigue experience are needed to clarify the multiple manifestations and meanings of fatigue.

Obviously the methodological difficulties encountered in fatigue research must be overcome. Of equal interest, however, are the questions raised with respect to theoretical and conceptual problems. A more refined theoretical approach may broaden insight into fatigue. An explicit definition of the concept of fatigue is often lacking and a wide range of operationalisations are used, frequently concepts such as malaise and weakness are used interchangeably as if they have the same meaning. Exploratory and descriptive work will culminate in concept clarification.

Little is known about the mechanisms that produce fatigue. Fundamental research is required to identify normal fatigue mechanisms. We need to learn how these mechanisms may be affected by disease or treatment states. Exacerbating this lack of knowledge are the numerous existing definitions of fatigue, and the difficulty in synthesising the fatigue literature across studies and disciplines. Studies are required which utilise or take into account theoretical explanations for fatigue and thus can validate, add to or refute factors proposed in various models and begin to provide an understanding of the mechanisms underlying fatigue in the cancer population.

In conclusion, fatigue is a major concern for the individual with cancer. Its prevalence and impact require that cancer nurse researchers devote more time to assessing this common phenomenon with methodologically sound studies. Since nurses are the primary health professionals involved in the identification and management of fatigue, serious research efforts must be concentrated in this area to provide an empirical base for clinical practice.

CHAPTER 5

METHODS

5.1 Purpose Of The Study

The purpose of the study was to monitor the subjective dimensions of fatigue in patients receiving cytotoxic chemotherapy as a treatment for cancer, and to provide a description of the relationships of a number of factors postulated to influence fatigue. In addition, the researcher wished to document the nature of any interventions utilised by patients in response to fatigue and explore the effectiveness of such measures. Hence, this study sought to increase the knowledge base concerning patients experiences in dealing with fatigue encountered during chemotherapy.

5.2 Aims

Several key areas were explored in order to fulfil the purpose of the study. The researcher sought to:

- Monitor the subjective dimensions of fatigue (including information concerned with the onset, pattern, duration, intensity and distress caused by this phenomenon), as documented by the subjects in a daily diary designed by the researcher, and maintained over the period of twenty-one to twenty-eight days following the administration of a pulse of chemotherapy.

- Describe the nature of the relationship between factors associated with fatigue in this patient population which may influence it, such as mood (as measured by the Mood Adjective Checklist (Lishman, 1972), symptom distress (as measured by the Holmes Symptom Distress Scale (Holmes, 1989), and a selection of demographic variables associated with this population such as the type, pattern and nature of chemotherapy drugs received, stage of disease and type of cancer.

- Describe the self-care interventions which patients utilise in response to fatigue and the perceived effectiveness and source of ideas for such interventions, through the use of the daily diary.

- Test aspects of reliability and validity of the instruments used in the description of fatigue and the other variables, namely, the Holmes Symptom Distress Scale (Holmes, 1989), Mood Adjective Checklist (Lishman, 1972), Fatigue Diary and the Piper Fatigue Scale (Piper *et al* 1989).

A glossary of terms developed for the study is contained in Appendix A.

5.3 Rationale For The Design

The study was developed from the review of the literature considering previous methods of measurement and in addition, from the researcher's clinical knowledge base. Previous methods of measurement were considered and the study approach was refined through a series of pre-tests and a pilot study of the selected instruments and design.

The problem of fatigue in a sick population has not been extensively researched as previously stated in the literature review. Most studies concerned with fatigue in clinical populations have adopted cross-sectional research designs. Consequently the knowledge base from which to plan and initiate care is fragmentary, research neither confirming nor refuting previously accumulated results. A number of research studies undertaken with cancer chemotherapy patients have produced cross-sectional data at predetermined intervals. Measures must be timed to document when fatigue develops in relation to treatment ; assumptions are often made about what occurs in the intervals between these measurements and an over-reliance on retrospective recall at interview is evident. Researchers risk missing important changes during intervals, including decline in health status which is later reversed.

The present study sought to overcome some of these drawbacks by employing a research design which would record trends and changes over time. However, it is crucial to consider the confines within which the researcher was working and the background to the current study prior to any description of the methods. Research into clinical nursing problems is acknowledged as being fraught with problems, and this study proved no exception to this. Conducting clinically focused research presents particular challenges when attempting to adhere to the rigours of scientific research. Difficulties are common in first acquiring a sample and then in retaining it, particularly when one is committed to a study which is longitudinal in nature. Many factors are influential which often lead to some compromises (such as frequency of instrument administration), often confined by the setting and the nature of the sample. Relatively little attention has been paid in the

past to the host of practical and logistical problems confronting researchers in cancer care, however these can have a significant impact on the integrity of the investigation (Van Dam, Linssen and Couzijn, 1984 ; Yates and Edwards, 1984 ; Van Dam and Aaronson, 1987).

In an area where there is a paucity of research, there is the temptation to attempt to answer a multitude of questions in one study through the collection of large amounts of data. This often results from the feeling that, due to the effort required to recruit and maintain the sample over a period of time, one should maximise the amount of information obtained from each subject. It is acknowledged that the generalisability and applicability of findings to clinical practice cannot be achieved from a discrete, single investigation. However, the present researcher was committed to a study that would ultimately influence the design of nursing interventions to assist in the palliation of this problem in the future.

A longitudinally designed study involves the use of repeated measurements on the same individual. The choice of this strategy is useful for detecting change in individuals or groups over time. The pre-tests and pilot study describe an approach to the development of a simplified method of determining fatigue and selected factors postulated to effect this phenomenon, in a busy clinical setting and in the participants' home. As a research tool a simple, rapid method would be useful in assessing the effectiveness of newly instituted nursing interventions particularly with potentially stressed and ill individuals.

The self-report mode of measurement possesses a number of unique advantages and characteristics to recommend it, as well as several inherent weaknesses. Self-report measures reflect information derived directly from the person experiencing the phenomena, namely, the patient himself. However, the self-report method tacitly assumes that the individual being assessed can and will accurately describe his current symptoms and behaviour, a premise which cannot always be supported. However, in justifying the use of self-report, the subjective nature of fatigue dictates that the sensation is only apparent to the person who is experiencing it . In spite of concerns about its deficiencies, the self-report method remains a useful form of clinical measurement and represents by far the best approach available. A structured diary requires only a few minutes to complete, participants are not burdened by the activity, and perhaps are more willing to complete serial administrations of the instrument over periods up to twenty-eight days in length. Of primary importance was the development of a patient self-report instrument that was comprehensive and robust while also being of sufficient brevity to be of practical use in the clinical setting.

A number of constraints were operating during the design and conduct of the study which should be reported. The level of tolerance of the participants to a research enquiry which involved repeated testing was of great concern to the researcher. Careful consideration was given to the total cumulative burden of data collection in relationship to patients, staff and the institution.

The researcher was acutely aware that completing a course of chemotherapy is a potentially stressful experience for many patients, encompassing physical and psychological strain, and she did not wish to add to this if at all possible. Research requires a sensitivity to the demands that a particular measurement procedure can place on subjects. This was counterbalanced against the importance of obtaining multiple measures of a given concept. This undoubtedly influenced the design and scope of the study and the recruitment of subjects to the sample, and may have led to the sacrifice of optimal measurement practices. Patients about to commence chemotherapy for the first time are acknowledged as being likely to be extremely anxious, and this would hamper any efforts by the researcher to inform potential participants about the study, as they would already have had to retain large amounts of new information. For this reason the number of first pulse participants recruited was limited to ten, and they were carefully screened. Refusals to participate may have been, in part , a function of the timing of the measurement. Subjects at this time may have been too emotionally distressed to make a decision whether or not to respond, or they may, because of other factors, not have the time or emotional energy to participate.

It would have been preferable to collect data over a complete course of chemotherapy which often entails six pulses. With the method selected this would have placed unfair demands on the subjects, in the opinion of the researcher. High attrition rates are likely and characteristic of longitudinal measurement efforts in that subjects agree to participate but when faced with actually responding decline by not completing the diary. Previous experience in using diaries as research instruments (Richardson, 1989) suggested that participants did not find the task onerous or difficult over the period of one month; on the contrary, many participants found that it was useful and provided solace. Patients often welcome the opportunity to report their experiences and concerns even within the confines of a formal research investigation.

Time was devoted to ensure the data collection procedures, to as great an extent as possible, were simplified and tailored to accommodate the clinical routine. This required a thorough knowledge of the range of clinical procedures, both diagnostic and therapeutic, around which cancer operates.

Research in cancer care and in particular cancer nursing research has blossomed in the last ten years. The implication of this is that the cancer patient population in the institution concerned were a potentially heavily researched group, and a decision was made not to approach any subjects who were presently enrolled in any other nursing research study.

5.4 Proposed Design And Conduct Of The Study

The proposed design was longitudinal and descriptive/correlational in nature. It was decided to gather information through the use of a semi-structured diary and the repeated administration of a number of self-report instruments designed to measure aspects of fatigue, mood, and symptom distress. The research design and data collection schedule were chosen with an emphasis on minimising patient, staff and institutional burden. A schematic representation of the initial design is presented in figure 5.1.

Completion of the diary occurred on a daily basis for a pulse of chemotherapy (the exact number of days was dependent on the protocol the participant was receiving). Each day the participant responded to items concerned with aspects of mood, symptoms, the dimensions of fatigue and self-care management strategies. At seven-day intervals - at the end of the first week following chemotherapy administration, at the approximate nadir, and just prior to the next cycle of chemotherapy - a further battery of instruments were included, a symptom distress scale, a more comprehensive fatigue scale and a mood checklist. This was done with the intention of expanding the depth and breadth of the data collected at times thought to be important in the development or abatement of fatigue. Hence, the choice of these assessment points was dependent upon both theoretical and practical considerations

The time frame within which the study was conducted can be found in figure 5.2.

A research assistant was available to assist with various aspects of the investigation. This was a valuable relationship developed since the inception of the project. She was familiar with the research strategy and her specific duties included assisting with data collection, data reduction and acting as a second person during data entry to monitor the process and verify correct data entry. The researcher and assistant

Figure 5.1 Proposed data collection procedure

	Day Post Chemotherapy**																				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21 *
Instrument to be completed																					
Diary																					
Participation Notes																					
Holmes Symptom Distress Scale																					
Mood Adjective Checklist																					
Piper Fatigue Scale																					

* This assumes a 21 days cycle of chemotherapy, data collection extends for those subjects receiving chemotherapy based on a 28 day cycle, at which point the final interview and Piper Fatigue Scale would be completed.

** Day 1 is the day the patient receives chemotherapy.

Figure 5.2 The time frame of the study

The study was conducted over 4 years

January 1991 - September 1991

Formulated research proposal.

Correspondence with researchers for the purpose of gaining approval to use instruments (Holmes, Piper, and Lishman).

Met physicians and nurses with clinical responsibility for oncology patients at the proposed site for data collection and obtained consent to approach patients under their care.

Prepared material necessary to present to the District Nursing Ethics Committee of the Health Authority concerned in June 1991.

Ethical approval was granted at the latter end of June 1991.

September - December 1991

Conducted pre-testing and pilot study.

January 1992 - February 1992

Reviewed results of pilot study and formulated the study design.

Preliminary data analysis and the design of coding frames.

February 1992 - December 1993

Commenced main study data collection whilst continuing to review potential methods of analysis.

1994/5

Data analysis and synthesis of the results.

Preparation of the written thesis.

met at regular weekly intervals to discuss various aspects of the research, including consistency in such matters as approaching participants and coding of the data.

5.5 Selection Of A Site For The Study

Subjects for the research study were recruited from an oncology unit situated within a large London teaching hospital. The oncology unit comprised an in-patient facility of twenty-six beds and a variety of out-patient clinics. These facilities were served by a team of specialist doctors and nurses who catered for patients during the diagnostic, treatment and palliative stages of disease. The chemotherapy suite, where patients would receive bolus and short-term infusional chemotherapy treatments was adjacent to the in-patient facility. In coming to the decision to select this site a number of factors played a role:

- The researcher had previously established links with this unit.

- It was estimated, with reference to previous treatment records, that a reasonable number of patients with a variety of cancer diagnoses would be expected to undergo chemotherapy in the period planned for the pilot and main study data collection.

- Treatment and care arrangements appeared to mirror those in other oncology units around the country.

- The consultant and senior nurse with responsibility for the care of cancer patients within the unit received the initial proposal enthusiastically.

- The unit was situated within a hospital within which the researcher worked for a large proportion of time each week. This was an important consideration if data collection was to be possible over a sustained period of time whilst the researcher continued to work.

- Current practices and research protocols appeared compatible with the proposed research, and no other large scale nursing research was being conducted with the proposed sample.

It was recognised that it would have been preferable to recruit patients from more than one site as this would have resulted in an increased rate of recruitment and thus a larger sample in the time available for data collection. However, due to the nature of the

design selected for the study increased human resources would have been necessary to collect data effectively from an additional site.

5.6 Selection Of A Sample

Initially it was planned to recruit a stratified convenience sample of approximately ninety patients who fell into a number of discrete groups who were about to, or were in the process of, receiving chemotherapy:

Thirty patients with a diagnosis of small cell lung cancer
Thirty patients with a diagnosis of lymphoma
Thirty patients with a diagnosis of breast cancer
Thirty patients with a diagnosis of a gynaecological malignancy.

In considering the nature of the sample a number of critical factors played a part:

- The sample should be large enough to facilitate the description of the variables under study considering that there was likely to be a wide degree of variability, and that this description would be possible with the proposed techniques for data analysis.

- The sample should reflect a variety of patient groups (males and females) who commonly receive chemotherapy for cancers of both a solid and haematological nature, at various stages of the treatment process.

- A random sample would not be possible as this would decrease the number of potential recruits in the time available.

- A variety of cytotoxic drugs should be given in a number of different combinations and schedules.

It was anticipated this would lead to potential variation in the dimensions of fatigue such as intensity, duration and frequency and other potential influencial variables such as age and sex, and produce sufficient numbers to allow statistical comparisons. It was hoped, if recruitment to each sub-group was successful, that this would allow comparisons between males and females and between different diagnostic categories.

In addition, to the points raised above, patients approached for recruitment met the following criteria:

- Age over eighteen years of age.

- A decision had been made by the physician in consultation with the patient that the patient was about to commence chemotherapy or was already in the process of receiving such treatment.

- The person was willing to participate in the study following a full explanation.

- The person was able to understand, speak and write English and had the ability to place an appropriate mark indicating a response on the scales selected for measurement purposes.

- The patient was considered by the oncology sisters to be both physically and psychologically capable of taking part in the study, and it was considered that this would not place an inordinate burden on the patient or his/her family.

Several concerns about the scope of the sample were raised by a statistician, particularly in relation to the likely variability within and between each diagnostic group. In a sample which is non-random with a consecutive series of subjects such variability would raise difficulties when interpreting the results. A number of suggestions were made:

- Increase selectivity in terms of the age range of subjects, for example, recruit subjects who only fall into the middle age range, not including relatively young or old subjects.

- Refrain from including any subjects who are receiving chemotherapy solely as a palliative measure.

- Limit to include subjects of one sex.

The researcher was concerned about maintaining a balance between adequate subject accrual and the necessity for selectivity to limit variability. It was proposed to remain flexible while examining vigilantly the potential subjects available, acknowledging it might be necessary to adjust stratification if it became clear some groups would be filled more easily than others in the time available. Attempts would be made to describe the groups carefully enough in terms of variability, informed by discussion with the clinicians. It seemed prudent at this stage not to restrict the wide

sample as few important factors had been consistently reported in previous studies to be related to fatigue .

One additional point concerning the sample related to the route of chemotherapy. Patients receiving oral drugs as their sole treatment were not included, but patients receiving a combination of intravenous and oral drugs were recruited as this type of therapy is often encountered in the lymphoma patients.

Despite these well-laid plans for sample selection, a surgical consultant with principal responsibility for breast cancer patients refused to grant access to patients under his care, and this had consequences in terms of subject availability. In addition, it soon became clear that recruitment, after two months into the main study, was not progressing as rapidly as the researcher would have preferred, or had previously estimated. At this stage the decision was made to alter sample selection and release some of the previously outlined restrictive criteria. The main change involved including patients receiving chemotherapy of a continuous nature for gastrointestinal/pancreatic tumours, a method of chemotherapy administration rapidly becoming established in this group of patients. No previous research on fatigue patterns had been carried out on this group of patients. Limited information exists on the toxicity profiles associated with this form of treatment. Sample recruitment was monitored closely during data collection and strategy reviewed as appropriate. It was acknowledged that there was a risk that the sample size of some of the groups might be insufficient for meaningful comparisons, however, it was important in the light of the research questions posed to recruit a sample which gave the researcher the chance of detecting variability.

A description of the chemotherapy protocols received by the study participants can be found in Appendix B.

5.7 Ethical Considerations

Institutional approval in principle for the study to be undertaken was sought from the District Nursing Research Ethics Committee. A proposal was submitted in June (1991) and approval granted in September (1991). As noted earlier the appropriate physicians and senior nurse were approached and permission gained to approach patients under their care. Written informed consent was sought prior to any patient commencing participation in the study. This was often a lengthy process and included explanations as to the purpose of the study, what was required of the participant and how the diary was to be completed (the patient information sheet offered to the potential participants and consent

form are contained in Appendix C). At this point the researcher maintained a degree of vigilance to cues that could indicate some anxiety or unwillingness to complete the study and participants were encouraged to express feelings to the researcher or her assistant if they were not happy with the undertaking, and emphasis placed upon the ability of the participant to withdraw at any stage of the study without fear of recrimination or prejudice. Assurances of confidentiality and anonymity in the written report were provided. Attention was paid at all stages of design, data collection and analysis to the Royal College Of Nursing document entitled "Ethics Related To Research In Nursing" (Royal College Of Nursing, 1993).

5.8 Negotiation Of Access

Access to the clinical area and potential participants were negotiated with physicians with primary responsibility for oncology patients within the proposed site, whilst pursuing ethical approval.

Following preliminary discussions and written communication the researcher met with two contrasting responses. The medical oncology consultant received the researcher with enthusiasm and support, whereas the surgical consultant with principal responsibility for breast cancer patients refused access to patients under his care. Reasons supplied surrounded the issue of patient stress at this particular time and the fact that he considered a large proportion of patients were already taking part in medical research studies.

A number of meetings were arranged with the medical oncology consultant, senior nurse and sister responsible for the oncology ward and nursing personnel involved in chemotherapy administration in the oncology unit. Professional links had already been previously established with the nurses concerned. The purpose of these meetings were to establish a relationship with the personnel concerned, to provide explanations about the study, allow opportunity for discussion, glean useful comments and answer any questions. Detailed written information concerned with the nature of the study was provided to medical and nursing staff to which they could refer to at a later date. The researcher was invited to attend a unit meeting attended by members of the medical and nursing team to present the proposed study and allow further opportunities for discussion. These meetings were felt to be extremely fruitful and constructive by both researcher and staff. Close liaison was necessary with the oncology sisters who were responsible for the organisation and administration of chemotherapy, as this facilitated identification of suitable participants on a day to day basis.

It became obvious after a number of days of data collection that a significant number of the lymphoma patients were cared for by an alternative consultant. To maximise chances of successful recruitment to each group, the consultant haematologist responsible for lymphoma patients in the oncology unit was approached. He gave his enthusiastic consent for the patients under his care to be invited to participate in the study.

5.9 Methods And Instruments Of Data Collection

5.9.1 Patient participation notes

Biographical details of relevance to the study were collected from patients' medical records and clarification sought from the relevant medical consultant when required. This information was recorded on the sheet entitled 'Patient Participation Notes' (see Appendix D).

5.9.2 Diaries

5.9.2.1 Introduction

The diaries referred to here are not those intimate journals persons ordinarily keep for their own private purposes, although such documents have been employed in sociological and psychological research (Allport, 1942). The term *diary* is used here to refer to an annotated chronological record or log. Individuals are asked to maintain a record over time according to a set of instructions. The use of structured diaries is contested. Allport does not include formally structured documentation as a true diary. Structuring, it is argued, forces the subject into a narrow view of their life events, decreasing spontaneity associated with this format (Burgess, 1984) .

Allport's (1942) classification places diaries into one of three categories;

- Intimate Journals : providing an account of thoughts, events and feelings that the individual perceives as important.

- Logs : a record of events, meetings and visits.

- Memoirs : similar to an autobiography, interpreted by the author retrospectively and providing an account of a particular social group or events.

Since Allport's classic review, a variety of forms have been developed. Diaries have been used extensively to register daily social interactions, in consumer expenditure surveys, and in studies of food consumption, use of travel and time. This discussion will be limited to health diaries. Use of a health diary (sometimes referred to as a health calendar) has been common in nursing practice. Nurses have incorporated the diary as a means of helping clients document their symptoms and factors which precipitated them, as well as recording parameters, such as fatigue or pain. To date there has been little exploration of this tool in a nursing research context yet the daily diary has been used as a data collection method in health services research since the early fifties. Recently this method has been revived in this literature with a particular interest in the diary's unique characteristics as a research instrument, in particular when compared to morbidity and utilisation surveys.

5.9.2.2 Data collection with diaries

To date health diaries have been used to describe an array of chronic and short term illness and behaviours. The nature of data collected with the health diary has varied with the purpose of the study. For example, some diaries have elicited data regarding days on which the respondent experienced symptoms, days on which the respondents were unable to perform their usual activities and days on which individuals engaged in self-care, health seeking behaviour, or took no action in response to symptoms (Banks, Beresford, Morrell, Waller and Watkins, 1975 ; Kasl, Gore and Cobb, 1975 ; Rakowski, Julius, Hickey, Verbrugge and Halter, 1988).

Freer (1980b) utilised health diaries over a period of four months in a study of the content and process of self-care practices of twenty-four women . The focus was on the common everyday health problems. Freer felt the diary would yield more information than a retrospective health interview while the time frame permitted the investigation of reactions in response to perceived health upsets. Diaries have been used to collect information about individual family members' health and illness behaviours (Roghman and Haggerty, 1972). Individuals usually report data for him or herself, although in some instances one person is asked to report for the entire family (Roghman and Haggerty, 1972).

The diary allows researchers to study health seeking behaviour as a multi-faceted construct, not merely as a reflection of the uptake of health services. Diary-use allows documentation of symptoms and associated coping strategies by the individual or family

experiencing them within their own frame of reference. Rakowski, Julius, Hickey *et al.* (1988) is an example of diary usage in this area. They documented the daily symptom experiences of older adults over a two-week period and the actions they initiated with a self-kept diary. The facility to monitor symptom experience on a daily basis is an important consideration for investigators who wish to study health-behaviour decision-making and care-seeking actions.

Rakowski, Julius, Hickey *et al.* (1988) suggest that monitoring on a daily basis permits the creation of indices reflecting multiple points of data as they actually occur, rather than relying on reports of usual behaviour or responses to proposed scenarios. Recall techniques are likely to produce under-reporting of short-term discomforts, nagging low grade chronic conditions and minor bouts of ill health. Individuals may also retrospectively define past episodes as having been serious or not serious depending on what long-term effects remain, rather than based on the discomfort or disruption of routine that occurred at the time of the episode.

Diaries may be used for a number of differing purposes including i) Methodological studies comparing prospective diaries to other retrospective data collection sources, ii) *Aides memoirs* to improve recall of events in a later retrospective interview, and iii) As a primary source of data (Verbrugge, 1980).

5.9.2.3 Advantages and disadvantages

Several advantages are associated with the use of a diary as a data collection procedure. Rich data can be obtained about an individual and family health processes surrounding health and illness and the decisions to seek help. The time sequence involved in the development of a symptom episode and the illness behaviour related to it can be documented, helping to determine the temporal relationship between the two events. A most important advantage is that the participant can prospectively unfold a series of events and perceptions relevant to their subsequent actions rather than rely on recall of past events (Allen, Breslow, Weissman and Nisselson, 1954 ; Roghman and Haggerty, 1972). In a series of Medical Research Council studies, which involved chemotherapy and radiotherapy for lung cancer, daily diary cards proved highly sensitive to day to day changes in symptoms (Jones, Fayers and Simons, 1987 ; Bleehen, Fayers, Girling and Stephens, 1989 ; Bleehen, Girling, Fayers, Aber and Stephens, 1991 ; Fayers, Bleehen, Girling and Stephens, 1991).

Disadvantages associated with this method include : expense in terms of interviewer time needed for instruction, follow-up and coding of the results, elimination of those participants who cannot read or write or those who choose not to keep the diary, inability of the researcher to immediately probe for additional data beyond that provided and linguistic biases dependent on the individual's education and literary background. Another important source of bias associated with this method occurs when an investigator studying families requests one member to report for others. Kosa, Alpert and Haggerty (1967) mention the possibility of mechanisms of censorship operating where respondents only record those symptoms which meet certain minimal requirements of severity and duration. The representativeness of the sample may suffer due to non-participation, failure to commence the diary, the omission of diary days or the suspension of diary completion.

Figure 5.3 Reported advantages and disadvantages when utilising diaries as research tools

Advantages

* Produce rich data regarding processes used to promote health and cope with illness in individuals over time
* Supports dynamic as well as static analysis
* Does not reply on retrospective reflection, thus reduces recall error
* Can be descriptive and intimate
* High levels of reporting achieved when compared to retrospective interviews
* A series of events can be documented and examined for causal relationships

Disadvantages

* Time required to instruct about tool and follow up
* Bias in that excludes participants who cannot read or write
* Inability of the interviewer to probe for further information, must be taken at face value
* Dependent on the motivation of participant
* Crucial data may be omitted/skipped
* Conditioning effects may occur
* Survey costs are high
* Data collection, processing and analysis may be complex

The advantages and disadvantages associated with the diary when utilised as a research instrument are summarised in figure 5.3. Verbrugge (1980 ; 1984) counters

many of the persistent arguments levelled against diaries as research instruments mentioned above by offering empirical evidence and solutions to problems often encountered.

5.9.2.4 Compliance and respondent co-operation

This type of data collection method obviously demands more time and effort on the part of the respondent than, for example, single interviews, and constitutes a clerical task to which people will respond with differing levels of skill and enthusiasm. The length of the data collection period for which diaries have been maintained spans from from one to two weeks (Kasl, Gore and Cobb, 1975) to over one year (Freer, 1980b). Several studies have used strategies such as remuneration, follow up telephone calls, follow up interviews and visits to collect diaries and checks for completeness. Financial remuneration may not be important in influencing the decision to participate, but probably influences commitment to complete the diary.

Norman, McFarlane, Streiner and Neale (1982) argue that there appears to be good reason to limit the total duration of diary usage. Initial compliance may be high amongst those who participate, but there is a consistent drop in the reporting of incidents with the passage of time. Bleehen, Fayers, Girling *et al.* (1989) reporting on the Medical Research Council Lung Cancer Working Party experience with daily diary cards revealed very poor compliance in this group. Specific centres contributed to the low rate. No reasons are offered. However, little effort appears to have been devoted to maintaining the sample, and the research team expected patients to complete cards from admission until imminent death. Roghman and Haggerty (1972) noted a decline in reporting during stressful events, and this may represent either a waning motivation to record data as time progresses, or may indicate that the participants' perceptions changed as the diary was kept. Mooney (1962) has attributed this to *fatigue*, a lack of willingness to complete the diaries in the same detail as time passes. Norman, McFarlane, Streiner *et al.* (1982) solution to this problem was to ask respondents to complete a randomly selected three-day block every two weeks. Additionally telephone contact was made forty-eight hours prior to the scheduled day of completion and lottery tickets were given. This combination of strategies maintained a high compliance in a study conducted over two years in a sample of over four hundred individuals.

Verbrugge (1984) considers attrition, task performance and conditioning effects and has made a number of recommendations about staff activities, diary format and field procedures with the ultimate goal of retaining members, improving record quality and reducing reactivity to the study.

Analysis of sample members with complete diaries may reveal particular characteristics. Carp and Carp (1981) revealed that attrition related to diary keeping resulted in under-representation of certain groups (e.g. low income, little education, minority ethnicity and poor health).

5.9.2.5 Format

Diaries are constructed according to one of two formats :

- As a journal where all health events are entered on the same page for each day
- As a ledger where separate pages are used for different types of events e.g. medication use and visits to the doctor.

Freer (1980a) provides useful information on the organisation, planning and management of a health diary study ; for example, it should be established that the respondent interprets the question in the same way as the organiser. Unstructured diary sheets in health research have been found to yield disappointing results. Structuring the situation as much as possible allows even the less articulate respondents to provide daily information, for example, by checking boxes. The respondent should be able to complete the diary in less than five minutes. However, there is little known about the technical aspects of design which aid respondents.

Patients may find a diary difficult to complete, any feature of the method which leads to non-biased participation will diminish a representative sample. Information about the characteristics of respondents and non-respondents may be usefully recorded. Its salience may lead to high co-operation in those most affected by the problem under investigation.

5.9.2.6 Reliability and validity

Diary strategies have been used relatively seldom, and little is known about their psychometric properties. However, as the method does not require the respondent to recall past events, it seems likely to provide more valid descriptions of minor and frequent events than the interview approach (Allen, Breslow, Weissman *et al.*, 1954) . In general diary errors usually involve incorrect or missing data, whereas interview error involves the participants telescoping events into smaller time periods (Roghman and Haggerty, 1972). These authors conclude that the diary is a more valid approach to

collecting data regarding the use of health services than interviews, particularly for time sequence data involving illness behaviour. The possibility of conditioning effects such as sensitisation and fatigue and mechanical response sets are discussed in the literature (Verbrugge, 1980).

Carp and Carp (1981) analysed five sets of data to assess the reliability, validity and generalisability of diary data. Results suggested that scores obtained from one-week diaries had satisfactory construct validity and that for salient activities they were less subjective to retrospective bias than interview data.

The quality of data provided seems closely related to the effort devoted by staff in encouraging diary keepers to maintain them, reducing missed pages, missing items and ambiguous entries. Validity is difficult to assess, but one strategy is commonly used to assess validity of self-reported health events : recordings may be compared with clinical and hospital records, thus producing an estimate of criterion validity, although this is only possible for health events that involve medical care. Interviewing respondents about events recorded in a diary within a given time frame can be attempted.

Reliability and validity estimates have been attempted by using different instruments to measure the same categories of events of concern to the researcher, such as health visits, daily activities or use of medications (Follick, Ahem and Laser-Wolston, 1984, for example). This approach has also been utilised when studying the utility of the daily diary card to study quality of life in patients receiving randomised trials of chemotherapy in breast and small cell lung cancer (Geddes, Dones, Hill, Law, Harper, Spiro, Tobias and Souhami, 1990 ; Fraser, Ramirez, Ebbs, Fallowfield, Dobbs, Richards, Bates and Baum, 1993). Small cell lung cancer patients used a diary comprising obligatory items (Geddes, Dones, Hill *et al.*, 1990), and the breast cancer patients were permitted to choose the most important items from four domains (Fraser, Ramirez, Ebbs *et al.*, 1993). In the former study comparison was made between the diary card, the European Organisation For Research And Training In Cancer Questionnaire (Aaronsen, Ahmedzai, Bergman *et al.*, 1993) and the Spitzer Quality Of Life Index (Spitzer, Dobson, Hall, Chesterman, Levi, Sheperd, Battista and Catchlove, 1981) and in the latter between the Qualitator (a daily diary card), Nottingham Health Profile (Hunt, McEwen and McKenna, 1985) and the Linear Analogue Self-Assessment (Priestman and Baum, 1976). These comparisons revealed expected convergent and divergent validity and demonstrated sensitivity of the diary cards to short-term changes when compared with other measures.

This strategy was used by Woods (1981). The criteria used for validation of the health diary included a recognised index of mental health (Cornell Medical Index M-R scale [Brodman, Erdman and Wolff, 1956]) and the individual's assessment of self-perceived health. The data obtained from family health diaries were compared with scores and self-ratings obtained during interviews. Symptoms reported in the diary were only weakly correlated with the scores from the Cornell Medical Index M-R scale and poorly correlated with a self-perceived health rating. This study demonstrates conflicting utility of the diary as a nursing research instrument. Many of the advantages noted by previous researchers are supported but a number of disadvantages are apparent. It appears to be a weak measure of mental ill health or poor health on this occasion, but persuasive arguments to explain why this may have occurred are suggested by the author.

5.9.2.7 Data analysis

Diaries provide a time series of data from each individual. This has enormous analytic potential for analysis of variations over the entire diary period and also day by day, making possible both individual-level and aggregate analysis. Data collection and processing are not intrinsically more complex. However, these activities may be more labour intensive than for other survey procedures, and the data more difficult to analyse. Missing data inevitably leads to problems in conducting statistical analysis, and as yet there have been few guidelines in the literature of how to deal with this (Fayers and Jones, 1983).

The analysis of health diary data have been examined in detail by only a limited number of writers (Spitzer, Dobson, Hall *et al.*, 1981 ; Fayers and Jones, 1983 ; Eckenrode, 1984 ; Machin, D'Arcangues, Busca, Farley and Pinol, 1987, for example). Verbrugge and Balaban (1989) through recourse to a recently completed diary study, identified techniques for visual and statistical analysis and concluded with a useful discussion of longitudinal data, noting special features of the data set and what to expect and learn from it.

5.9.2.8 Diaries in nursing research

There has been little exploration of this tool in a nursing research context, and the research activity of gaining data over time has not proved popular with many nurse researchers. The following studies highlight the use of diaries with the cancer patient population.

Oleske, Heinze and Otte (1990) discuss the rationale and methodology of diary data collection with an ill population, focusing on an experience with a sample of cancer patients receiving domicillary nursing care. Diary recordings were obtained and evaluated in order to gain insight into the nature and magnitude of health problems encountered in the home by individuals with cancer. A monetary incentive was offered. It was noted that the sheer volume of patient recording made it apparent that the issue of respondent burden need not be of great concern with the use of such an instrument. Oral comments given by diary keepers to research assistants, when calling to instruct the recorders indicated that they found keeping diaries a helpful outlet. Data collection therefore appears feasible for longitudinal research of older individuals with a chronic condition such as cancer . In this study less than 5% of the sample were receiving active cancer treatment during data collection. In general the researchers felt that diaries could be useful data collection methods in measuring the quality of life over time with chronically ill elderly individuals. Utilising the diary method of data collection can assist in identifying the subtleties of health problem variation among people with advanced cancer and also may pave the way toward developing new strategies for improving quality of life.

The diary as a record of health related events was used by Frank-Stromborg (1986) to investigate the health promotion behaviours in the ambulatory cancer patient. This approach to data collection was selected because of its suitability for symptom disability and health action reporting. The researcher examined cancer clients' self-care and health promoting activities. The diary employed daily ratings, closed responses and open ended questions in attempts to evaluate what ambulatory cancer clients do to make themselves feel better. The author claimed that a health diary would result in high levels of reporting, sensitivity to detail, reduction of memory recall bias and the ability to accurately reflect individual daily reports of health and health actions.

Faithfull (1992) reports the use of the diary method when investigating the experiences of individuals after cranial radiotherapy. The diary provided a suitable method for eliciting the experiences of participants. Data from the diaries provided the basis for semi-structured interviews and produced a descriptive account of the phenomenon of somnolence syndrome.

Dodd has initiated a series of studies to examine the self-care practices of chemotherapy and radiotherapy patients through which she developed a self-care behaviour log (Dodd, 1984c ; Dodd, 1984b ; Dodd, 1987 ; Dodd, 1988a ; Dodd, 1988b ; Dodd, 1990). The studies were published in sequence and explored differing aspects of a

general focus concerned with determining the nature and frequency of self-care behaviours initiated to alleviate side-effects. One of the most recently reported studies (Dodd, 1988b) intended to replicate and extend previous research (Dodd, 1982b ; Dodd, 1982a ; Dodd, 1983 ; Dodd, 1984a), incorporating earlier recommendations, and attending to some of the previous methodological weaknesses, hoping to provide further understanding of the frequency and nature of self-care behaviours and influencing factors. The inclusion of the self-care behaviour log rather than a retrospective questionnaire, to eliminate reliance on recall, is of relevance to the present discussion.

In the log, patients record each side-effect as it is experienced indicating the date of onset. They also record the severity and distress experienced (two five-point scales), the self-care behaviour undertaken to alleviate the side-effect, perceptions of the effectiveness of each self-care behaviour (rated on a third five-point scale) and their sources of information for each self-care behaviour. Versions of this log have been utilised in the study of preventive self-care in relationship to potential side-effects (Dodd, 1984c), and in the evaluation of the efficacy of providing proactive information on self-care performance in patients receiving radiotherapy and chemotherapy (Dodd, 1987 ; Dodd, 1988a).

Unfortunately there is minimal discussion on aspects associated with compliance and missing data due to toxicity of side-effects . In one of the later studies mention is made that thirty-eight out of eighty families who were approached did not complete the study (Musci and Dodd, 1990). Reasons for non completion included complications of treatment or disease, incomplete questionnaires and death of the patient. Most patients were hospitalised for complications resulting from side-effects at some point in time .

Data analysis in all studies is limited. It is invariably aggregated to produce various ratios of the self-care behaviour log, quantifying the frequency, effectiveness of self-care activity, and overall management of the experienced side-effects. Time as a variable is only considered when determining the relationship of the duration of experienced side-effects to initiation of self-care behaviours (delay in initiating behaviours). The reliability of the log could benefit from further testing together with some attention to measures to explore validity, but the utility has been demonstrated in enabling the self-report of symptoms.

Nail, Jones, Greene *et al.* (1991) using a self-care diary developed for the study, asked a sample of fourty-nine patients with cancer to record their side-effects, rate the severity of each side-effect, and report on the use and efficacy of self-care activities two and five days after treatment. In contrast to Dodd's approach this team of investigators used a

closed approach whereby the side-effects and the corresponding self-care activities were listed in the diary for the respondents to make their selection. The subjects in this study reported greater use of self-care activities than the subjects of Dodd's studies and this discrepancy may be due to the difference in the approach used to collect data on self-care activities.

5.9.2.9 Section summary

Diaries seem to be as flexible, and in principle, as widely applicable research instruments as questionnaires and interviews in the circumstances described above. The issue is not one of feasibility, but the relatively high cost, the greater degree of co-operation required from the respondent, and the vastly increased work involved in the complete analysis of all the data collected. Although used infrequently in nursing research studies with patients who are undergoing active treatment and potentially unwell, the present researcher considered that the diary method appeared to be a potentially efficient and sensitive tool with which to reveal information about fatigue, self-care practices and other variables such as symptoms and mood state in the clinical and home environment.

5.9.2.10 Diary for the present research

The diary was designed to elicit information concerning the daily degree, intensity and severity of fatigue, and patient initiated interventions performed to help the participant cope with fatigue during the previous twenty-four hours. It was envisaged that the diary would yield data which would illustrate the potential for interventions in relation to the experience of fatigue. The research design required an approach that established whether fatigue existed and that recorded the experience of the affected individual. It is divided into two parts and consists of a number of elements (see Appendix E for the final version adopted):

(A) Six visual analogue scales exploring mood, appetite, sleep and nausea (added after pre-test).

(B) Four visual analogue scales representing various dimensions of the fatigue experience (only 3 included in the pretest version, dealing with extent, severity and distress) and checked boxes to confirm the presence of fatigue at specific times of day.

(C) A record for patients to document any actions performed to relieve fatigue, their effectiveness (rated on a four-point scale) and the source of the idea. This portion of the diary was a self-report instrument adapted from the questionnaire and log of Dodd (1982a; Dodd, 1983) designed to elicit information concerning self-care actions taken by patients in a previous twenty-four hour period.

(D) Open-ended items eliciting ideas about the contributory causes of fatigue and any other symptoms experienced that day.

Element A comprised the first section. Elements B, C and D comprised the second section, and were only completed if the respondent had experienced fatigue that day.

Scoring of the diary was by measurement of each visual analogue scale (VAS), and a coding system was developed to record the presence or absence of fatigue at various times of the day, performance of self-care behaviours and description of the open-ended responses. A measure of internal consistency was used to examine the relationship of one diary variable with a corresponding diary variable measuring the same factor, fatigue. More information on these aspects is contained in the section on data analysis.

The diary was to be completed by the person receiving chemotherapy, although it was acknowledged due to possible debilitating side-effects, that on some occasions another person may complete the items with the patient giving the information.

The researcher had previous experience with this method of data collection with patients receiving chemotherapy (Richardson, 1989), and it was felt that daily completion over a period of approximately one month would not place an undue burden on the participants, even though the respondent might be suffering from fatigue. A copy of the instructions for diary completion were bound inside the front cover. This included a sample recording of a VAS. However, no examples of self-care activities were included to avoid suggesting certain strategies. The development of a usable and reliable format of the diary is reported in the pilot work. Consideration was given to achieving a non-threatening appearance and facilitating easy completion, recognising that these features may discourage participation.

5.9.3 Visual analogue scales

5.9.3.1 Introduction

When a researcher is interested in determining the intensity or magnitude of patients' sensations, perceptions and subjective feelings and the relative strength of their attitudes and opinions about specific stimuli, the VAS has been utilised as one approach to permit the scaling of such stimuli. Such scales have been acknowledged as quick and easy to use in the clinical setting and have often been the preferred type of scaling technique in ill populations. In particular they are suitable for monitoring progress over time (Gift, 1989b) and have been used extensively as a self-report device in both descriptive and experimental nursing research when considering such phenomena as emotional distress, dyspnoea and nausea (Janson-Bjerklie, Carrieri and Hudes, 1986 ; Sutherland, Walker and Till, 1988 ; Edwards, Herman, Wallace and Pavy, 1991).

These aspects particularly drew the present researcher to considering their utility for the current study, as an approach to measuring a number of the dimensions of fatigue, a variety of other symptoms particularly associated with cancer and its treatment, and aspects of mood.

Some complex problems relating to the use, accuracy, reproducibility and statistical analysis of the results obtained from VASs are well recognised, and some of these will be considered below.

5.9.3.2 Design and construction

VASs (sometimes referred to as linear analogue self-assessment scales [LASA scales]) employ a drawn or printed line of a specified length, with verbal anchors at each end, to represent a subjective state or stimulus, such as pain (Carlsson, 1983, for example); dyspnoea (Gift, 1986 ; Gift, 1989a, for example); anxiety, depression and other aspects of mood and psychological distress (Luria, 1975 ; Cella and Perry, 1986); fatigue (Piper, Lindsey, Dodd *et al.*, 1989, for example); well being (Clarke and Spear, 1964) and quality of life (Priestman and Baum, 1976). Detailed advice on the technical construction of such scales is offered by Cline, Herman, Shaw and Morton (1992).

Typically, a 100 mm line anchored by words or short phrases is used and it can be drawn either vertically, or more traditionally a horizontally orientated scale is used. The vertical format may be preferable, since a vertical line is more directly analogous to

"more" at the top and "less" at the bottom, hence being more sensitive and easier for subjects to use (Gift, Plaut and Jacox, 1986). Scott and Huskisson (1979) and Gift (1986) report the vertical format may eliminate difficulty with problems in the left-right discrimination and adds to the sensitivity of the scale. However, each format is reported as being equally valid. On the other hand, Dixon and Bird (1981) report that horizontal lines appear less subject to respondent error attributable to the angle at which the scale is viewed.

In a unipolar scale the anchors depict the extreme limits of the sensation or response to be measured, such as "no fatigue" on the low end of the scale and "fatigue as bad as it can be" on the upper end. The end phrases should not be so extremely worded as never to be employed. The end anchors should allow for the entire range of sensations regarding the phenomenon being studied, so that limits of responses are not externally constrained (Lee and Kieckhefer, 1989). A bi-polar scale can be used to measure mood with a line labelled, for example, "depression" on one end and "elation" on the other. Normal mood is assumed to lie somewhere around the midpoint between these two extremes. Gift (1989b) notes that many researchers studying the same phenomenon do not agree on the wording or what constitutes an extreme of a sensation and this hampers comparisons.

The subject is instructed to place a mark on the line corresponding to the intensity or quality of the subjective sensation/feeling being experienced. Some subjects appear unable to use a VAS successfully (Kremer, Atkinson and Ignelzi, 1981) and it is often advised that it is helpful to add a written example of how to mark the scale. Subjects may experience difficulty in converting a subjective sensation to a straight line, or the activity may be too abstract, particularly in the elderly patient population. Experience suggests that this disadvantage may be overcome by teaching subjects to use the scale or providing detailed written instructions (Lorig, 1984 ; Guyatt, Townsend, Berman and Keller, 1987). Prior to a patient using a VAS at home, it is sensible that he or she fills one out under supervision - if this is not adhered to many will forget and not understand the concept of the scale. Using this regime Scott and Huskisson (1976) found failure to be very unusual. Visual and motor faculties are needed for successful completion, and in the very old and very young such scales may not be suitable, nor where fine discrimination is required and the participant suffers from a hand tremor. In addition, to instructions on the technique for placing a mark on the line, the directions must specify a temporal or geographic reference to maintain consistency across subjects, for example daily - in the last 24 hours or now - at this moment. Once the respondent has demonstrated the ability to use the technique, multiple scales can be completed rapidly on repeated occasions.

Multiple VASs have been used to measure multiple constructs in a study or used as a response format to produce a summative score on a given phenomenon. VAS items have been used to study individual aspects of quality of life in cancer patients as well as combined to form an overall quality of life score (Padilla, Presant, Grant *et al.*, 1983). An important characteristic, especially when the research is concerned with an acknowledged multidimensional sensation, is that a VAS only measures one dimension of the phenomenon at a time, for example its strength or intensity. However, Cella and Perry (1986) draw our attention to the fact that the dimensions selected may share variance that can affect statistical tests.

5.9.3.3 Scoring

The scale is scored by measuring the distance in millimetres, generally, from the low end of the scale to a specified place on the subject mark, often the extreme bottom or left margin of the mark. This last point is crucial to ensure consistency in scoring. Rules should be established before scoring begins as potential errors can occur when quantifying marks and the reliability of data conversion should be documented. It is important to realise that photocopying the scale can cause small alterations in the length of the line, therefore printing is preferable to produce reliable measurements (Bloomfield and Hanks, 1981 ; Lorig, 1984).

Holmes (1989) cautions when utilising a number of VASs to investigate a phenomenon, that it must be recognised that although scores on individual items can be added to give a total score, this may be inappropriate since the scores obtained on a VAS do not provide true scores, but rather provide a rank order of their importance to the patient (Abdellah and Levine, 1986). Thus, although it can be said that a patient scoring thirty has more distress from a particular symptom than one with a score sixty, it is not possible to say how much greater is his degree of distress. Thus she concludes that such scores are most useful in providing within-subject comparisons over time.

A weighting system has been considered by Priestman and Baum (1976) when producing a composite score on quality of life. All factors are assigned equal weighting, but in reality it is likely that patients assign different weightings to for example, hair loss and an inability to do housework. This may result in some cases a fall in a score in one item being compensated by an improvement in an ability to do something or in the intensity of another symptom. Some events or symptoms may have far more significance for one patient than another but a reliable weighting system would be difficult to develop and introduce. This problem of *pooling* scores is not unique to multi-item VASs.

Statistical tools can be used to evaluate which variables are more important in discriminating between groups, such as discriminant analysis, logistic regression and multiple regression.

5.9.3.4 Analysis of visual analogue scale data

The level of measurement at which the data should be considered for the purposes of statistical analysis is subject to some controversy. Carlsson (1983) considers that they do not qualify as interval level scores and are not suited for the operations of addition or calculations of averages. Other researchers argue that the data could be considered interval or that they are at the ratio level of measurement (Maxwell, 1978 ; Price, McGrath, Rafil and Buckingham, 1983 ; Burns and Grove, 1987). Aitken (1969) considers that they provide quantitative, interval-level data that allows greater variance of responses and data that are more likely to be normally distributed. As described by Maxwell (1978), if the method is understood by the subject it seems appropriate to assume the scores represent at least ordinal measurement within a given subject.

Markings that divide lines into two portions give rise to a multinomial distribution of the proportions, which are often skewed to one or other end. Transformation is performed to normalise skewed distributions so that the necessary assumptions of parametric statistics can be met. Bond and Lader (1974), when utilising these scales in rating subjective feelings revealed that when the frequency distribution of each scale was computed and plotted, some were skewed towards the positive end, with a peak around the centre (social desirability may indeed be a plausible explanation for the skewness of several scales towards the positive end), skewness in this case was corrected by a $\log_e$ transformation. Priestman and Baum (1976) and Aitken (1969) both applied the arcsin transformation to compensate for skewness in distribution. Boyd, Selby, Sutherland and Hogg's (1988) data were highly skewed with a unimodal distribution, where most scores indicated normality or absence of a symptom, and in this case no single transformation would convert all the data items to an approximate normal distribution, and in this study they utilised non-parametric statistics and box plots, a tool used frequently in exploratory data analysis.

Aitken and Zeally (1970) argue that measurement to the nearest millimetre provides a sufficiently large number of categories to allow considering it as a continuum, and the scores meet the assumptions of parametric statistics . Aitken (1969) considers the critics to be wrong in arguing that a fine resolution is not permitted because it exceeds the discriminatory power of the rater both to appreciate his feeling, and to convey it with this

type of perceptual motor task. Thus most frequently the data are handled by parametric methods and more sensitive parametric techniques can be used including analysis of variance (Joyce, Zutshi, Hrubes and Mason, 1975), and principle component analysis (Bond and Lader, 1974), to facilitate these the scores are sometimes transformed. However, amongst statisticians the strongest support is to consider the data as ordinal, and Scott and Huskisson (1976) feel it is safer to treat the data in this manner and use non-parametric methods of analysis. Maxwell (1978) provides a strong case for researchers to have valid reasons in their own setting for using a transformation and presenting the distribution, medians and range of raw scores. As stated earlier he believes if the scale is properly understood and properly used the data must be at least ordinal within a single subject, but notes the results are often not treated as within subject data, they are grouped or pooled for between-subject analyses. He demonstrated that different methods of handling the results (parametric v ordinal ; within-subject v between subject) produced varying degrees of accuracy and sensitivity. It can be concluded that the theory surrounding the analysis of VASs still seems poorly understood. Decisions made by the present researcher concerning the issues raised above are detailed later in the chapter in the section concerned with analysis.

5.9.3.5 Psychometric properties - reliability and validity

This method of measurement is advocated as possessing a certain sensitivity to subtle fluctuations, and reliability and validity are often similar to more time-consuming and complex measures (Cella and Perry, 1986).

Reliability of VASs is most frequently assessed using the test-retest method, but stability over time can only be appropriately assessed when the phenomenon itself remains stable within the time intervals selected. Correlations between two administrations have been moderate to strong (Clarke and Spear, 1964 ; Aitken, 1969 ; Padilla, Presant, Grant *et al.*, 1983). A problem with using test-retest reliability with VASs is that unless the variable being measured is a trait, low reliabilities are likely to occur.

Revill, Robinson, Rosen and Hogg (1976) addressed the reliability of the scale as a method of assessment, firstly, in relationship to visual and motor co-ordination; that is , the ability of the patient to place a mark where he or she intends to put it, and secondly, testing the presumption that the same rating would be given for the same memory of pain on more than one occasion. The VAS in these circumstances demonstrated good reliability.

When considering other types of reliability, unidimensional VASs are limited by the fact that internal consistency reliability cannot be assessed with a one-item measure. Congruity of response across multiple bi-polar scales assessing a single concept provides evidence of internal consistency, but this is seldom documented. Interrater reliability can be estimated when more than one person is involved in the scoring process.

Respondent bias may be minimised by constructing some of the VASs with reverse end anchors, as bias is possible when people associate high scores with a more positive response and low scores with a more negative response, but the necessity to alternate the favourable extremes of the lines in this manner has not been confirmed. Ballatori, Roila, Basurto*et al.* (1993) provide evidence that it is preferable that the semantic polarisation be the same for all the items e.g. the positive semantic value should always be on the right or left of the VAS, regardless of whether it is "very much" or "not at all".

When the VAS is used for repeated measurements, it has been debated whether to show subjects their previous markings. Some researchers advocate allowing subjects to see their previous scores, whilst others do not (Scott and Huskisson, 1979 ; Dixon and Bird, 1981 ; Guyatt, Berman, Townsend and Taylor, 1985). Dixon and Bird (1981) asked the question that if a patient claimed pain on consecutive occasions and had access to the initial results, would the error involved in reproducing the result be the same along the length of a 10 cm VAS ? Scott and Huskisson (1979) had previously shown that there was a tendency to overestimate pain severity when the initial result was not available, in Dixon and Bird's study the tendency to overestimate when access to the initial reference line was given was even more pronounced and reproducibility was found to be variable along its length (subjects were better able to reproduce marks near the extreme ends of the scale and hence reproducibility is related to the intensity of the sensation experienced). Despite the preceding discussion Luria (1975) feels that these scales lend themselves to repeated use with patients. Success in recording change may be related to the patient populations studied, stable measurements are likely to be obtained in chronic patients with little changing sensations.

Validity of VASs has been assessed using several techniques. The majority of investigators who have evaluated the validity of the VAS have utilised a criterion-related approach. Criterion-related validity (concurrent and predictive) can be documented by significant correlations between the VAS and alternative measures of the phenomenon whenever such measures exist (for example depression, using the Beck Depression Inventory [Little and McPhail, 1973]). Acceptable levels of concurrent validity have

been reported for both affective states and sensations (Aitken, 1969 ; Cella and Perry, 1986). Construct validity using the contrasted groups approach has also been established for some VASs measuring mood and quality of life (Padilla, Presant, Grant *et al.*, 1983), comparing well subjects and chemotherapy patients. Visual analogue scales have been used when validating the various dimensions of phenomena, such as the sensory and affective dimensions of pain, illustrating that distinct dimensions of an experience are measurable by this technique (discriminant validity). Content validity may be gauged by examining the extent to which multiple bi-polar scales are representative and inclusive of the phenomena being measured.

5.9.3.6 Sensitivity

Compared with measures that require subjects to rate intensity of their moods, feelings, or sensations on a categorical scale or checklist, VASs do not limit subjects to a limited number of possible responses, but allow them to place their response at any point on the continuum. It is often argued that because of this property VASs are more sensitive than categorical scales (Joyce, Zutshi, Hrubes *et al.*, 1975 ; Ohnhaus and Adler, 1975 ; Huskisson, Jones and Scott, 1976) and that they may avoid some of the pitfalls of language associated with graphic rating scales and the assignment of individual interpretation to descriptors (Sriwatanakul, Kelvie, Lasgna, Calimlim, Weis and Menta, 1983).

The use of more than twenty divisions on a VAS would lead to an apparent increase in sensitivity. Scott and Huskisson (1976) suggest there must be a limit to the size of differences that patients can discriminate, and the use of twenty divisions has received some support.

However, such sensitivity may be a liability due to the ceiling effect encountered with some subjects when measuring change over time (Little and McPhail, 1973). Borg (1982) compensated for this by opening up the upper end of the scale and allowing patients to indicate amounts higher than the maximum. Gift (1989b) thus recommends that when such sensitivity is desirable or essential, provision be made for subjects who record sensations at the maximum and later perceive them to be worse. Maxwell (1978) documented that some subjects hesitated to use the extremes of a VAS, and recommended in order to maintain sensitivity that the raw scores be converted to a proportion of the maximum score indicated by each subject

It has been argued that these scales do not allow comparison since they lack numerical values. Thus although they can indicate that there is, for example, more or less pain, they fail to indicate the extent of the change, and as a result cannot be used in empirical studies (McCorkle and Young, 1978). Aitken (1969) points out there is no claim that the use of an analogue scale permits liberal comparisons, as the transfer function is not known, the same word used by different people need not convey that they experience the same feelings, neither does comparable positioning of marks on lines. However, comparisons can be achieved with greater sensitivity than with semantic phrases, particularly between different occasions in the same person. Others however suggest that such scales reduce the difficulties of response sets and the artificial distribution of positive and negative responses (Joyce, 1968). In addition, since the subject is not restricted to direct quantitative terms he can make as fine a discrimination as he wishes, thus clearly differentiating between the responses to individual items, rather than being forced into artificial response categories.

5.9.3.7 Section summary

VASs as a technique have been noted as holding several advantages, particularly when attempting to measure subjective feelings for clinical purposes. The VAS has been primarily used to gather information about feelings, perceptions, or sensations that are difficult to measure on scales with predetermined intervals. They are easy to understand, simple to administer and score, and can be completed quickly. Studies indicate that sensitive, reliable and valid measures can be obtained (Selby, Chapman, Etazadi-Amoli, Dalley and Boyd, 1984). These features appear to make the VAS an attractive measurement option for the clinical researcher concerned with maximising the amount of data in relationship to subject demand. However, it is prudent to recommend that the validity and reliability of the VAS be evaluated with each particular situation and with multiple strategies; that statistical methods for handling scores are considered carefully in the light of the comments in the literature; and any researcher should be aware of the pitfalls and controversies surrounding their use.

5.9.3.8 Visual analogue scales used in the present study

In the present study a number of the reported dimensions of fatigue, aspects of mood and a selection of symptoms (nausea, sleep and appetite), estimated with VASs were completed on a daily basis. The Holmes Symptom Distress Scale was completed at seven-day intervals which also utilised VASs as the method of quantification. A detailed discussion on the measurement of fatigue is contained within the literature review, and the development of the diary reported elsewhere in this chapter. The researcher selected the term fatigue rather than tiredness as the anchor for the relevant visual analogue scales in the diary. The term fatigue was not defined for the participants, rather they were instructed to complete these scales according to their own perception of this phenomenon.

5.9.4 Symptom distress scales

5.9.4.1 The concept of symptom distress

Rhodes and Watson (1987) review the concept of symptom distress and comment that it is a concept that has not been clearly defined or delineated, but describe symptoms and/or feeling states as "phenomena experienced by a person and not directly observable by another, with symptoms only becoming known through the report of the person being assessed" (p.242). Symptom distress is also the physical or mental anguish or suffering that results from the experience of symptom occurrence and/or the perception of feeling states. Distress is another component of symptoms that can best be measured with self-report tools. A commentary on the methodological issues surrounding the measurement of symptom distress has been produced by McCorkle (1987). It is well established that symptom distress assessments are usually self-report measures. When patient perceived health or symptoms have been validated against a health professional rating of patients' symptoms, divergent results are often evident.

5.9.4.2 Instruments available to measure symptom distress

A variety of instruments are available but there are very few symptom scales that have been designed specifically for cancer patients; however a number of measures developed are applicable to the problems patients with cancer experience such as the Brief Symptom Inventory (Derogatis and Melisaralos, 1983), Symptom Profile Instrument (King, Nail, Kreamer *et al.*, 1985), Sickness Impact Profile (Bergner, Bobbit, Carter *et al.*, 1981) and the Rotterdam Symptom Checklist (de Haes, Van Knippenberg and Neijit, 1990). These

instruments reflect scales at different stages of development, have been used in studies with cancer patients and can be used both as clinical and research tools.

5.9.4.3 Instrument used in the present study

The Holmes Symptom Distress Scale (HSDS) was selected for the present study in preference to those mentioned above as the items included were considered useful to the needs of the research project, and the tool had been used previously in a British population similar to the present study. A short time was required for completion which was an important factor, as this scale would not be the only one completed on repeated occasions.

The Symptom Distress Scale (a linear analogue self-assessment scale, LASA) which has been modified by Holmes and her co-workers (Holmes and Dickerson, 1987 ; Holmes, 1989), from that developed by the Americans, (McCorkle and Young, 1978) was utilised in the present study (see Appendix F). Items included in the scale are pain, nausea, appetite, sleep, mobility, appearance, diarrhoea, constipation, tiredness, concentration and mood.

5.9.4.4 Development of the scale

The original purpose of McCorkle and Young in developing the scale was to identify concerns of patients receiving active cancer treatments in a medical oncology clinic. Two pilot studies were conducted. The first study ($n=26$) sought to identify human concerns of patients who were receiving active cancer treatments (Schneider, 1978). The types of symptoms identified in this study were similar and mirrored those identified in previous studies, such as those by Twycross (1972) and Hinton (1963). The second pilot study ($n=60$) had the purpose of developing a symptom distress scale which could facilitate measurement of the degree of distress perceived by the patient (McCorkle and Young 1978). The majority of the sample had cancer or another chronic illness. Initially eight symptoms were included: nausea, mood, appetite, insomnia, pain, mobility, fatigue and bowel pattern. Concentration and appearance were added as the investigation proceeded. It was recognised by the authors that the scale did not include all possible symptoms, but rather the symptoms of concern to patients. Initial validity and reliability were established at this point and the scale demonstrated face and content validity for specific symptoms.

The method involved the use of cards, each one with a single symptom, on a scale from one to five (as illustrated in figure 5.4). Ten cards representing the ten symptoms were given to each patient, one at a time, in a consistent order.

The reliability of the scale was estimated by computing Cronbach's alpha which was .8, indicating a high degree of reliability. A correlation matrix was generated, revealing that all correlations were found to be positive. Symptoms demonstrating higher than a .5 zero order correlations of interest to the present study were fatigue and mood; fatigue and appetite; fatigue and insomnia. There were a number of others. The authors suggested factor analysis should be performed in later studies to identify if underlying constructs could be identified.

Figure 5.4 Symptom distress card for fatigue

Each of the following cards lists a different statement. Please take your time and think about what each statement says. Then place a circle around the number that most closely measures what you are experiencing today on a scale of one to five. For example, number one would indicate no problems in regard to that particular statement and number five would indicate a maximum amount of problems. Numbers two through four would indicate you feel somewhere in between these two extremes.

Please put a circle around the number that most closely measures how tired you are feeling today.

Could not feel more tired 5 4 3 2 1 I am not tired at all

Source: McCorkle,R., and Young,K. (1978). Development of a symptom distress scale. Cancer Nursing, 1 (5), p. 375.

Subsequently the scale was revised and used with lung cancer and myocardial infarction patients (McCorkle and Benoliel, 1983 ; Donaldson, McCorkle, Georgiadou *et al.*, 1986 ; Kukull, McCorkle and Driever, 1986). McCorke and Benoliel (1983) identified and compared levels of symptom distress for patients with advanced lung cancer and advanced heart disease. The study thus described the level of symptom distress, current concerns and mood disturbance in persons with a diagnosis of one of two

life threatening diseases at two occasions. Data on symptom distress were obtained using an expanded version of the original scale, additional items were included to reflect the symptoms persons with lung cancer may experience such as cough and dyspnoea, and descriptive words for each numerical indicator were added. Cronbach's alpha on this occasion was estimated to be .79 at time one (one month post diagnosis) and .78 at time two (two months post diagnosis) and stability estimated using a test-retest method a coefficient of .78 was obtained. The original version of the scale has been used extensively in cancer nursing research and now has established reliability and validity, and can discriminate between heart patient survivors and cancer patients and appears sensitive to change in patients' symptoms.

5.9.4.5 Format

The scale is based on a linear self-assessment scale and respondents rate the degree of distress due to the symptoms common to cancer patients. Each item is represented by a title and a 100 mm linear analogue scale, each end of which is anchored by descriptive phrases, the right hand end of the line representing *normality* (i.e. the absence of a symptom) and the left the opposite extreme or state. Participants are asked to place a mark across the line at the point which most closely represents how they perceive their distress from each symptom at the time of assessment.

5.9.4.6 Scoring

Scores for each symptom are obtained by measuring from zero to the point (in millimeters) where the mark crosses the line. Zero represents extreme distress and the higher scores indicate less distress from individual items. The scale is most valuable in providing comparisons for each symptom in individuals over time, as a positional rather than a true score is obtained, but composite as well as individual scores for each item can be produced. The numerical value given to the visual scales provides the means by which individuals and sub-groups within the sample can be compared.

5.9.4.7 Studies examining psychometric properties of the instrument

Holmes (1989) compared the results to those obtained by McCorkle and Young (1978). On this occasion a pilot study with thirty patients was carried out, not with the purpose of outlining the tool's statistical properties, but, instead evaluated issues related to

administration of the tool, its acceptability and feasibility. She suggested that this indicated that the modified scale was no less effective in assessing symptom distress but that it had considerable advantages due to its simplicity and ease of administration. Following this pilot study, with a sample of one hundred and twenty cancer patients (a heterogeneous cross sectional sample), further reliability and validity testing was executed, demonstrating a marked similarity between the different cancer patient populations. The estimate of Cronbach's alpha on this occasion was .97. Forward stepwise multiple regression was used to explain the variation in the total scores obtained and principal components analysis to identify groups of symptoms supportive of the validity of the instrument.

Holmes and Dickerson (1987) compared the LASA version and likert type scales, where the symptom distress scale was part of a more comprehensive quality of life scale. Questionnaires based on a linear analogue, five point and six point scale were developed. At each end of the scales were written statements representing the possible extremes of the subjective responses to particular questions. The different types of questionnaire were allocated on a random basis to a sample of seventy-two cancer patients. Each patient completed two out of the three variety of forms separated by a period of 1.5 hours. Test-retest reliability was established for all forms of the instrument, for individual items and total scores. The highest reliability coefficient was obtained using the LASA (.97, $p < .001$) whilst the six point scale produced the lowest coefficient .72, $p < .001$). There was no statistical basis for selecting one scale in preference to another. However, the LASA was associated with fewer problems associated with administration and allowed greater flexibility and discrimination between responses to individual items. Cronbach's alpha for the symptom distress portion of the scale was .9. The correlation matrix yielded several interrelated areas of concern, for example, those between pain, nausea and tiredness. The authors suggest that the questionnaire could allow the presence or severity of such distress to be identified and an analysis of individual symptoms, or the relationship between symptoms, could provide valuable information which would enable care to be planned more effectively. Further results with the Quality Of Life Scale have been reported (Sutcliffe and Holmes, 1991) in inpatients and outpatients undergoing radiotherapy demonstrating differences between the two patient populations, illustrating the tools sensitivity/discriminatory ability.

Content validity has been established through reference to previous literature (McCorkle and Young, 1978 ; Schneider, 1978), comparison to previous findings (Holmes, 1989 ; Holmes and Eburn, 1989) and consultation with a panel of experts consisting of clinical practitioners closely involved in this area of practice. A series of

studies have now been published documenting various aspects of the instrument's validity, reliability and usability.

Holmes (1991) reports a preliminary investigation into the incidence of symptom distress in chemotherapy and radiotherapy patients and discusses further evaluation of the tool. The scale was found to be reliable and valid for use in both populations and the results indicated that although overall symptom distress is similar between both groups, there is considerable variation in the extent of that distress and the symptoms causing distress may differ between the groups.

Holmes and Eburn (1989) compared fifty-three cancer patients and their nurses' perceptions of symptom distress. The scale was simultaneously completed by the nurses caring for the patients, who were asked to rate the patient according to how they perceived he/she was feeling with regard to each particular symptom. Surprisingly, the trend was for nurses to overestimate the degree of distress when this was compared to the patients self-assessment. There were significant differences between the nurses' and patients' perceptions of the level of symptom distress, particularly with regard to the less visible symptoms.

5.9.4.8 Section summary

Holmes's work has illustrated that the scale is acceptable to patients, easy to use and quick to score. The previous studies have identified the best method of using the scale. To minimise bias standardised instructions should be given to all participants. A sample question should be used to demonstrate the method of completion. Reliability has been found to be high based on a measure of internal consistency. The scale is believed to possess content validity as it includes symptoms identified as major causes of concern to cancer patients and evidence is available to support construct validity. When attempting to assess subjective feelings it is often difficult to validate their depth and there are few accepted criteria against which to judge empirical data. The studies cited have gone some way to establish the validity of the scale.

5.9.5 Measurement of mood

5.9.5.1 Mood disturbance in cancer patients

The potential relationship between fatigue and mood has been documented in the review of the literature. Treatment for cancer is often associated with significant physical and psychological distress. The negative impact of cancer diagnosis and treatment upon mood state, and a general level of psychological distress is well documented, and a tremendous amount of work has been carried out in the last twenty years (Taylor, Lichtman, Wood, Bluming, Dosik and Leibowitz, 1985, for example).

Patients with cancer have to come to terms with the knowledge that they have a life-threatening disease and must develop strategies to cope with treatments. This can disrupt economic, social and sexual functioning and frequently cause anxiety and depression. The origin of such mood changes in the cancer patient is multifocal and persistent in origin, such as the diagnosis itself, changes in an individual's biopsychosocial condition, lifestyle alterations and dependence on health professionals (Welch-McCafferey, 1985). Negative affect rarely occurs in isolation, rather a constellation of multiple interrelated problems often occurs. A patient's emotional status is closely bound to other psychosocial events set in motion by the trajectory of the disease (Mathieson and Stam, 1991).

Much effort has been devoted to monitoring the nature and extent of psychological ill-health resulting from cancer and its treatment. Jacobsen and Holland (1991) analyse the diagnosis and treatment of cancer in terms of its stressful properties and review the literature on this topic reporting that estimates of emotional distress and psychiatric symptomatology are varied.

Emotional distress is an understandable and, perhaps inevitable reaction to the diagnosis of cancer. One of the most widely quoted studies in an evaluation of two hundred and fifty new admissions to three cancer centres, indicated that the prevalence of psychiatric disorders was 47% among new admissions of cancer patients (Derogatis, Morrow, Fetting, Penman, Piasetsky, Schmale, Henrichs and Carnicke, 1983). The most frequent disturbances were of anxiety or depression.

5.9.5.2 Instruments used for mood measurement in cancer patients

Three behavioural or psychological methods of measuring mood and affect exist: self-report scales, observer assessed psychiatric rating scales and scales derived from the content analysis of verbal behaviour (Gottschalk, 1984). There are a number of widely used and well-validated self-report measures of mood and affect. The Profile Of Mood States has norms for cancer patients and will be discussed in greater detail shortly. The Hospital Anxiety and Depression Scale (HADS) was developed by Zigmond and Snaith (1983) for detecting states of depression and anxiety, specifically for use with physically sick populations, and is also reported as a reliable instrument for screening for clinically significant anxiety and depression. A further advantage of the HADS is that it is extremely easy and quick to administer, complete and score and has been validated for use with cancer patients (Razavi, Delvaux, Farvacques and Rabaye, 1990 ; Moorey, Greer, Watson, Gorman, Rowden, Tunmore, Robertson and Bliss, 1991 ; Watson, Greer, Rowden, Gorman, Robertson, Bliss and Tunmore, 1991).

Other widely used continuum and categorical scales of depression and anxiety have been developed and include the Beck Depression Inventory (Beck, Ward, Mendelson *et al.*, 1961) and the Spielberger State Trait Anxiety Scale (Spielberger, Gorsuch and Lushene, 1970) and The Brief Symptom Inventory (Derogatis and Melisaralos, 1983). However, most have been designed initially for use with non-medically sick individuals, so threshold scores may require adjustment. A better way to screen for a mood disorder in cancer patients is by means of the HADS. Its advantage over the other self-assessment questionnaires is that the items contained within the scale deal with emotional, not physical symptoms.

5.9.5.3 Some issues in the measurement of mood in cancer patients

Recent reviews suggest that serious disturbance is confined to a small proportion of cancer patients (Mathieson and Stam, 1991). Control for stage of disease, type of patient problem on admission and the timing and manner of assessment may account for variable estimations reported in the literature. Several diagnostic instruments for research purposes have been developed based upon the DSM-III-R criteria (American Psychiatric Association, 1987) a psychiatric rather than a psychologically based or psychosocial assessment. The period during and following diagnosis is one of great flux and also may account for the variety of percentages reported. The studies which rely on primarily psychiatric diagnoses report much higher rates of distress than those using other criteria (Holland and Rowland, 1989). In contrast to the above approach a variety of studies have

employed standardised scales to assess negative affect and psychosocial problems such as the Profile Of Mood States (POMS) (McNair, Lorr and Droppleman, 1992 revised) and The Centre For Epidemiological Depression Scale - the CES-D scale (Radloff, 1977), and neither assessment tool assumes that the reference group to which patients should be compared is psychiatric patients. For studies using the above approach, reported rates of depressive symptomatology fall in the 10-30% range (Weisman, Worden and Sobel, 1980; Wellisch, Guidera, Pasnau and Fawzy, 1983 ; Cassileth, Lusk, Strouse, Miller, Brown, Cross and Tenaglia, 1984 ; Cassileth, Lusk, Brown, Cross, Walsh and Hurwitz, 1986 ; Stam, Bultz and Pittman, 1986). In fact, several of these studies have confirmed that psychopathological symptoms were absent or within normal limits for oncology patients (e.g. Cassileth, Lusk, Strouse *et al.*.

An immense difficulty when assessing patients who are physically ill is that many of the somatic symptoms (headaches, sweating, tremor and palpitations, appetite changes, insomnia) used for a diagnosis of depression and / or anxiety may be due in part to the cancer itself or due to the treatment. Some clinicians have suggested, therefore, that more emphasis should be placed on the non-somatic components of mood disorders when assessing patients already in a physically compromised state due to cancer (Plumb and Holland, 1981). Separating psychological state from physical symptoms which co-occur with the disease is problematic, both are likely to be in flux during the diagnostic and treatment phases.

5.9.5.4 Instrument selected for the present study

The Mood Adjective Checklist (MACL) adapted by Lishman (1972) from the earlier version of the POMS by McNair and Lorr (1964) was selected for use in the present study to measure mood changes (see Appendix G). It is a short version of POMS which is British in origin The checklist consists of twenty-four adjectives, randomly ordered, each requiring a response in one of four columns headed "not at all", "a little", "quite a bit" or "extremely". A scoring system of 0, 1, 2, 3 respectively is used to quantify responses.

McNair and Lorr (1964) made the distinction between mood and emotional state. Although they viewed them as overlapping categories they suggested that mood states are likely to be more persistent. They regarded mood as a concept with the status of an intervening variable. It was conceptualised "as an organismic state definable in terms of the antecedent inducing operations and the correlated behaviour consequences". Events

such as illness have been shown to be antecedent conditions inducing mood change as indicated by the MACL.

In selecting the MACL as oppose to the HADS, the focus of the former instrument is emotional well being rather than solely anxiety and depression. It has the capacity to detail a number of transient fluctuating distinct mood states. The physical feelings of fatigue and vigour related to the present research interest, and offered a means of estimating the construct validity (convergent and discriminant) of the visual analogue fatigue scales.

5.9.5.5 Use of adjective checklists in research on mood

A discussion will follow of the history of adjective checklists, and in particular the POMS from which the MACL was developed. Aitken and Zeally (1970) in a review on the measurement of moods, comment that "Moods are frames of mind, states of feeling that derive from emotional experience. Feelings themselves are individual and unique, and with certainty we can discern only our own" (p.215). Moods and feelings defy absolute measurement, measures reflect the mood or feeling state, they do not measure the mood in any specific unit. Depression and anxiety are not the only emotions synonymous with mood disorder: other important aspects of adjustment might be neglected. Typical emotional responses to cancer include anxiety, guilt, anger and hostility (Weisman and Worden, 1976-77).

A multitude of scales have been devised in questionnaire form to be completed by patients themselves, some of which have already been mentioned. Mood checklists have been developed principally in the United States and arose with the need for a quick method of assessing different mood states over varying time intervals, initially to evaluate the results of psychotherapy and pharmacological agents. The rationale for adjective checklists is based on respondents' individual preference for an inferred meaning given to different words. They are an attempt to include a variety of words to enable the respondent to express their own feelings in their own familiar terms. A thorough review of such studies using mood adjective checklists is beyond the scope of the present report. Studies in the literature using mood checklists have been largely derived from the Green - Nowliss (Nowliss and Nowliss, 1956 ; Green and Nowliss, 1957 ; Nowliss and Green, 1957) research which reported a factor analysis of their adjective list in which they isolated eight factors and demonstrated the adjective checklist was useful in quantifying mood changes induced by various experimental variables. Nowliss (1965) discusses methodological aspects of the use of adjective check lists to describe and measure mood

and in a further review concluded that they provide a quick, convenient method for assessing the current mood of the subject. The greatest drawback is that a subject will only convey how he thinks he feels, or possibly what he thinks he ought to feel, or wants the researcher to believe he feels.

Zuckerman (1960) developed and validated an adjective checklist for the measurement of anxiety in college students. The Multiple Affect Adjective Checklist (MAACL) is self-administered and measures the three affects of anxiety, depression and hostility. Test-retest reliability coefficients for the state measures are reported as low, which is expected, since moods vary from day to day. The test takes five to ten minutes to complete (Zuckerman and Lubin, 1965).

The POMS was originally developed in the 1960's, and later refined for marketing by McNair, Lorr and Droppleman (1971) to assess mood change over brief time intervals in individuals undergoing drug therapy and psychotherapy. A panel of psychiatrists selected adjectives from a pool which they agreed to be descriptive of the hypothesised mood/affective states of anxiety, fatigue, depression, hostility and vigour. The scale represents the refinement of these different adjective scales by means of repeated factor analysis. Data from the patient normative samples have produced highly satisfactory stability and test-retest reliabilities. McNair and colleagues have demonstrated both predictive and construct validity.

POMS provides an assessment of an individual's current emotional state by asking subjects to rate how applicable sixty-five different mood descriptions are to them. Subjects are given semantic differentials (a five-point rating scale), e.g. phrases such as "not at all" through to "extremely", which permit them to express the degree to which items such as "sad" apply. There are six different subscales on the POMS : tension-anxiety, depression-dejection, anger-hostility, vigour-activity, fatigue-inertia and confusion-bewilderment. Work has shown good specificity on the POMS subscales (the ability of the measure to identify correctly different populations, as opposed to sensitivity, which is the ability of an instrument to accurately pick up changes) and careful statistical analysis identified the underlying dimensions of mood being measured to establish the scoring categories. It now exists in a long (sixty-five items) and short (thirty-five items) form. Mood reactions can be estimated for example during the "past week including today" and for shorter periods such as "today" and "right now".

A total mood disturbance score (TMD) is obtained by summing the scores of tension-anxiety, depression-dejection, tension-anxiety, fatigue and confusion-bewiderment, and subtracting vigour. The scale thus has no natural zero, since it includes

a reverse-scored subscale of positive items and the total score may be positive or negative.

Concurrent validity of the POMS has been examined through correlation studies with similar types of instruments. Correlations between the POMS with conceptually similar instruments lends further support to the validity of this instrument. Independence of the different mood factors was demonstrated by Nowliss (1970). Norcross, Guadagnoli and Prochasks (1984) further examined the factor structure of the POMS and concluded that the instrument appeared internally consistent, multidimensional in nature with a relatively stable factor structure. However, they recommended caution in the separate scoring and interpretation of several of the scales.

There have been numerous studies using the POMS to measure/determine mood disturbance caused by the physical and psychological effects of cancer (Weisman and Worden, 1977 ; Bloom, 1982 ; McCorkle and Benoliel, 1983 ; Taylor, Lichtmain and Wood, 1984 ; Cassileth, Lusk, Brown and Cross, 1985 ; Taylor, Lichtman, Wood *et al.*, 1985 ; Holland, Korzun, Tross *et al.*, 1986). It is considered a standardised measure of psychological distress. Other studies have used the POMS to determine how the quality of life for cancer patients can be improved through self-help groups (Spiegel, Bloom and Yalom, 1981) and more recently when exploring the relationship between the empathy skills of primary nurses and the distress levels of their primary patients (Reid-Ponte, 1992). In general, it seems that cancer affects mood states and POMS profiles often indicate higher levels of depression-dejection, tension-anxiety, fatigue, confusion-bewilderment and total mood disturbance than other patient groups. However, cancer patients' scores remain within normal limits, although McCorkle and Benoliel (1983) reported that cancer patients experienced more mood disturbance, on the average, than heart attack patients.

The POMS was administered to patients receiving different chemotherapy drugs for small cell lung cancer patients (Silberfarb, Holland, Anbar, Bahna, Maurer, Chahinian and Comis, 1983). Those receiving combination chemotherapy containing Vincristine suffered significantly more depression and fatigue. This drug has acknowledged neurological toxicities and the resulting fatigue may be the effect that the drug has on central neurotransmitters.

The association between two primary covariates, extent of disease and performance status rating and the outcome of psychological distress in patients with small cell lung cancer has been studied using POMS as a measure of psychological distress (Cella, Orofiamma, Holland, Silberfarb, Tross, Feldstein, Perry, Maurer, Comis and Orar,

1987). Performance status and extent of disease appeared to hold a statistically significant association with reported distress on the POMS and could under certain circumstances be considered predictive risk factors for distress after cancer diagnosis.

Development of the POMS short form has been based on a need for a form that is easier to complete. This form is used quite often with the elderly and with those recovering from surgery. The POMS short form consists of thirty items and the same six scales as measured by the long form. A number of short forms exist (Shachman, 1983 ; Malouff, Schutte and Ramerth, 1985 ; Cella, Jacobsen, Orav, Holland, Siberfarb and Rafla, 1987)

The feasibility of using a short form in cancer patients is reported by Shachman (1983), whose impetus for the development of such a scale was the finding that when administering the tool it could take as long as fifteen to twenty minutes. The short scales were formed using the reliability programme of SPSS. Items were eliminated according to a two-fold criterion : i) The contribution to internal consistency of the scale, and ii) The face validity of the items in relation to the scales. Results demonstrated that the POMS (thirty-seven items in this case) could be shortened significantly without losing information or internal consistency.

An even shorter version (eleven items) was developed by Cella, Jacobsen, Orav *et al.* (1987) in a very large population of cancer patients. The Total Mood Disturbance Score was considered a useful starting point from which to construct a brief reliable measure of general mood disturbance or distress. A one factor solution was specified using principal components analysis, and items comprising this factor were then compared for their concordance to the overall mood disturbance score. The results provided supportive evidence for using the brief eleven-item measure of mood disturbance as a reliable index, with justification provided for using this form when the measurement of general distress alone is the goal.

5.9.5.6 The dimensions of the instrument for the present study

The five mood factors of the MACL are depression (represented by eight adjectives) and tension/anxiety, anger/hostility, vigour/activity and fatigue/inertia, each represented by four adjectives.

The dimensions of mood are:

Depression-Dejection
Depression accompanied by a sense of personal inadequacy

Tension-Anxiety
Heightened musculoskeletal tension including reports of somatic tension and observable psychomotor manifestations.

Anger-Hostility
Anger and antipathy towards others

Vigour-Activity
Vigorousness, ebullience, and high energy

Fatigue-Inertia
Weariness, inertia and low energy level

McNair and Lorr (1964) utilising repeated factor analysis (a series of six factor analyses were performed in the construction of the instrument) , conducted a series of studies which tested for the existence of a set of hypothesised mood factors, and determined their sensitivity to brief drug therapy. They found that these five mood factors varied more or less independently and scores were sensitive to change and largely independent of a social desirability set. Two additional moods of friendliness and confusion were identified but have not been confirmed as independent factors. All five factors have been postulated to be relevant to the experience of fatigue. Vigour is said to be a factor reflecting positive mood, whereas the others reflect negative states.

5.9.5.7 Use of the instrument in previous studies

The MACL has been used in a number of previous nursing studies. Wilson-Barnett (1977) examined patients emotional responses to barium x rays (barium meal and barium enema) in a quasi-experiment testing the effect of informing patients about barium x-rays on their emotional reactions. The MACL was used as the self-report scale of emotions. The researcher compared the level of anxiety reported by the informed patients with that of the control subjects who did not receive this information. Anxiety was the emotion of chief concern in this study. However, it was decided that all the adjectives would be used

for the study as they would potentially act as effective masks to the exact purpose of the study. Measurement was carried out on four occasions : on the day prior to the x-ray early in the afternoon, after the visit of a second researcher (blind to the group to which they had been assigned) later on the day prior to the x-ray, within half an hour prior to the x-ray, and within half an hour after x-ray. An experimental group of patients received an explanation of the x-ray procedure and the feelings it might cause and they compared with a control group who received no information. For the barium meal patients, no differences were found between the two groups at any stage regarding anxiety, but for barium enema patients, anxiety scores were significantly higher during the investigation itself. Informed patients receiving the barium enema reported less anxiety during the x-ray than controls, while control subjects' anxiety scores before and during the barium enema were significantly higher. The instrument was used again by the same researcher in 1981 when assessing recovery of post operative cardiac patients in the year following surgery. In this study it required careful thought by subjects to complete the MACL, but they felt able to do so.

Openshaw (1984) selected the MACL as the measure of affect in a descriptive correlational study concerned with the clinical judgement of nurses and the appraisal of patient affect, compared with the patients self-rating. The methodology employed rating by eighty nurses and one hundred and forty (medical and surgical) patients. The patients rated the checklist to describe how they felt that day and the nurses rated it as they considered that their patient felt. Webb (1984) in a descriptive and experimental study designed to collect information about recovery from hysterectomy and to test the effect of an experimental counselling session on this process, considered all five dimensions of the MACL to be relevant to this group. A number of standardised measuring instruments were utilised, including the MACL. Measurements were carried out in hospital in the early post operative period and again four months later. Depression scores fell over this time period, anxiety and fatigue were also reduced, while vigour and hostility levels were increased. Webb (1984) reports that the MACL proved satisfactory and women found it quick and easy to use, the adjectives often linking with their own experience. Intercorrelations between the dimensions and the other scales utilised were in the expected directions, adding confidence to the validity of the scales.

In a small study ($n=20$) Dawson (1991) investigated patients' perceptions of wellbeing following treatment for ovarian cancer. She obtained data for comparison to the previously mentioned study.

5.9.5.8 Reliability

Test-retest reliability is not an appropriate estimate of reliability in a state measurement of mood and would not be expected to possess a high temporal stability, as mood is a dynamic and changeable phenomenon over a relatively short period of time. Internal consistency, however, could be estimated but has not been reported in previous studies. McNair and Lorr (1964) showed that moods fluctuated over four to eight week periods according to whether patients were undergoing psychotherapy or not and Wilson-Barnett (1977) demonstrated its sensitivity to change over a four to six week study period. The original test-retest reliability for the factors were in the range of $r = .61$-$.69$ and internal consistency estimated using the Kuder-Richardson 20 formula between .8 and .92 Internal consistency has been improved in later versions of POMS ranging from .87-.95 (McNair, Lorr and Droppleman, 1992 revised)

Johnston and Hackmann (1977) asked questions concerning the repeated use of mood questionnaires on the same subject at weekly and daily intervals, an issue pertinent to the present study, and examined using the State-Trait Anxiety Inventory, Multiple Affect Adjective Checklist and the Lorr, McNair and Weinstein (1964) mood scale. Firstly, "are corresponding moods and mood changes correlated across questionnaires ?", and secondly, "do response sets affect the changes in responses?". Both within and between-subjects designs were used. The results suggest that the corresponding mood measures change in parallel, giving evidence of validity, especially for anxiety measures. Response sets (acquiescence and extreme responding) were evident with the Lorr scale scores but this effect was reduced in a within-subjects design. If used on a daily basis consideration should be given to the use of different versions.

5.9.5.9 Validity

Wilson-Barnett (1977) has confirmed the validity of the checklist in a British sample when factor analysis was carried out to establish that the adjectives were associated with the five factors found by McNair and Lorr (1964).

Openshaw's (1984) analysis involved factor analysis on both the patient and nurse data to investigate the similarity of interpretation of the adjectives between the two groups in terms of the derived factors prior to further analysis. Principal components with iteration and an orthogonal varimax rotation was computed. The factors that were derived were identical to those derived in the previous work (Wilson-Barnett, 1977), but

there was dissimilarity in terms of the number of adjectives subsumed under the factor "depression".

Lishman's MACL (Lishman, 1972) correlated significantly with several other measures. For example, depression correlated with Beck Depression Inventory Scores. Items from the POMS checklist sometimes reflect the physical concerns of patients on treatment: "unable to concentrate, restless, worn out, fatigued, exhausted and bushed". The assessment may lead to exaggerated levels of symtomatology at the time points of beginning and during treatment, especially with psychiatric measures not designed for chronic illness populations.

5.9.5.10 Social desirability

Nowliss (1965) suggests that the influence of a social desirability response set has less influence when an individual is asked to judge his present mood than when asked to report typical mood. When he tested a mood adjective checklist for social desirability set he found very small correlations. McNair and Lorr (1964) found that the mood scores had low correlations with the Crowne Marlowe Social Desirability Measure (Crowne and Marlowe, 1960) and thus seem to remain independent of social desirability.

5.9.5.11 Scoring and analysis

Non parametric tests are suitable for use with the MACL as the tool generates ordinal scores. The use of procedures which utilise ranking tests are appropriate, and averages should be expressed as medians. In tests using ranks, many score the same, and corrections for ties may need to be made.

On attempting to score the Mood Adjective Checklist it became evident that this procedure was potentially complicated. The researcher was unsure whether the scores to the positive items of the vigour /activity subscale should be subtracted or whether the scoring system should be reversed when dealing with these items in order to arrive at a composite score. This would influence the mean total score. No light was shed on this issue after revisiting the original research articles. The researcher wrote to Professor Lishman to seek some definitive guidance. He advised against summing the scores to obtain a total mood disturbance score and suggested the scores for each of the mood states be analysed separately (Personal Communication, 1992). Thus the five dimensions of mood as appearing in the Mood Adjective Checklist would be correlated in turn with

the items concerned with fatigue in the diary, particularly the vigour/activity and fatigue/inertia elements to examine aspects of validity (convergent and discriminant).

5.9.5.12 Section summary

The instrument had been originally developed in relationship to studies of psychopharmacology and the consistency of the conceptual orientation of the tool could be challenged. However, through continued use in other patient groups beside psychiatric patients its usefulness has been demonstrated, and there is no assumption that the tool assumes that the reference group to which patients should be compared are psychiatric patients. Evidence has been presented for factorial and concurrent validity (particularly with the Beck Depression Inventory of the mood factors [Lishman, 1972]) , and sensitivity to change and patients' willingness to complete serial administrations of the instrument (Wilson-Barnett, 1977). It meets the demand for a rapid, economical method of assessing such transient, fluctuating affective states.

5.9.5.13 Visual analogue scales used in the diary for daily mood measurement

The use of the MACL on a daily basis would have proved cumbersome. However, it was considered important to obtain some brief measures of certain aspects of mood every day. This would enable the researcher to look for associations and patterns between the dimensions of fatigue and mood. A number of VASs were selected to document the intensity of three affective states on a daily basis in the diary.

- A bi-polar scale with a line labelled "calm" at one end and "anxious" at the other
- A bi-polar scale with a line labelled "happy" at one end and "sad" at the other
- A uni-polar scale describing ability to concentrate

Crawford Little and McPhail (1973) consider the VAS when used in the rating of depression to be one of the quickest single methods whilst maintaining optimal sensitivity, and a reliable measure of this mood state when compared to the Beck Depression Inventory. The use of the VAS to measure moods is supported by Aitken and Zeally (1970), who view feelings as dimensions which are continuously variable: researchers should resist division into discrete steps.

In attempting to develop a streamlined measurement method to evaluate emotional distress, a six-item linear analogue (items were concerned with fatigue, anxiety, confusion, depression, energy and anger) self-assessment scale derived from the POMS was developed and tested on sixty cancer patients (Sutherland, Walker and Till, 1988). The specific purpose of the study was to develop a feasible and reliable LASA scale for use in a busy outpatient setting that would identify cancer patients' emotional distress. Results indicated that such an instrument was both feasible and reliable, and preliminary evidence of validity was demonstrated using the original version of POMS. Further exploration of validity has been undertaken (Sutherland, Lockwood and Cunningham, 1989). The use of analogue scales in rating subjective feelings is reported by Bond and Lader (1974). Cella and Perry (1986) used three VASs to measure anxiety, depression and distress. Test-retest reliability coefficients, correlations within analogue scales, and correlations between analogue scales and standardised measures of anxiety, depression and distress provided preliminary evidence to support the use of VASs when other standard measures are unfeasible, such as the burden of completing longer questionnaires. They concluded that these scales seemed capable of measuring feeling states in a quick reliable and relatively sensitive manner. This is consistent with the findings of Little and McPhail (1973) who reported that similar analogue scales were reliable and valid global measures of mood.

5.9.6 Piper Fatigue Scale

5.9.6.1. Introduction

The measurement of fatigue is covered in some detail in the literature review, hence the development of the Piper Fatigue Scale (PFS) will not be discussed here. It was selected because of its suggested ability to measure multidimensional aspects of fatigue and its specificity to the cancer patient population. It was expected to play a fundamental role in describing fatigue. However, as will become clear when the reader consults the pilot work, it failed to fulfil the researcher's expectations.

5.9.6.2 The instrument format

The self-report instrument contains fourty visual analogue scale items measuring four dimensions of subjective fatigue : the temporal dimension (five items), relating to the timing, frequency, pattern and duration of fatigue; the intensity/severity dimension (twelve items), relating to severity, distress and degree of disruption in activities of

living; the affective dimension (five items), relating to the emotional meaning attributed to fatigue; and the sensory dimension (nineteen items), relating to the physical, emotional and mental symptoms of fatigue. Four additional open ended items measure the perceived cause of fatigue, perceived relief measures, additional fatigue descriptors and associated symptoms (the original form of the instrument may be consulted in Appendix H).

5.9.6.3 Scoring

Individual subscale and total fatigue scores are calculated (range 0–100). Subscale scores are calculated by summing the scores on all items within a particular subscale and dividing the sum by the number of items within the subscale. This gives a mean subscale score for the subject and keeps the subject's score on the original 0–100 scale. A total fatigue score is calculated by adding the four subscale scores together and dividing by four.

5.9.6.4 Psychometric properties

The development and initial testing of the instrument has been reported by Piper *et al* (1989) and Piper (Personal Communication, 1992) in two cancer samples. Reliability and validity estimates have been calculated for breast and lung cancer patients receiving chemotherapy. In these samples internal consistency reliabilities (Cronbach's alpha) range from .80 - .95; concurrent validity estimates (correlations between PFS, Fatigue Symptom Checklist and Profile of Mood States scores) are moderate to strong.

5.9.7 Hospital Anxiety And Depression Scale

5.9.7.1 Introduction

As will be described, during the pilot work phase and in the early stage of the main study the PFS did not live up to expectation and was abandoned. This presented the researcher with the opportunity to introduce a further instrument into the study at the end point of data collection. The Hospital Anxiety and Depression Scale (HADS)(Zigmond and Snaith, 1994) was readily available and with a reputation for accurately identifying states of anxiety and depression in subjects with a physical illness (as it does not include items

of a somatic nature which could be caused by physical disease as much as mood disturbance) suggested it could provide a valuable comparison with the MACL.

5.9.7.2 Format and Scoring

It consists of two subscales - one measuring anxiety (A-scale) and one measuring depression (D-scale) which are scored separately (see Appendix I). The test consists of fourteen items, seven for each subscale, and patients rate items on a four-point scale. Individual items are scored from 0–3 to 3–0 depending on the direction of the item wording. Instructions emphasise that the state to be recorded on the questionnaire is the state 'over the last few days'. The Depression and Anxiety subscale scores are determined by adding the numbers in the D and A columns respectively. Interpretation of the scores is possible by reference to the manual (Snaith and Zigmond, 1994) where 0–7 = normal, 8–20 = mild, 11–14 = moderate and 15–21 = severe.

5.9.7.3 Psychometric properties

Unlike most other scales the HADS is derived from clinical experience rather than factor analysis and its development is described by Zigmond and Snaith (1983). Subsequent studies of the HADS have established its psychometric properties. The internal consistency of the two subscales was established by Moorey, Greer, Watson *et al.* (1991) on the replies of five hundred and sixty-eight people with cancer. Cronbach's alpha was .93 for the A-scale and .90 for the D-scale. The construct validity of the scale as a measure of two factors was also confirmed in this study. Two independent factors emerged which accounted for 53% of the variance. However, the bi-dimensionality of the scale has not been replicated in a sample of French patients (Razavi, Delvaux, Farvacques *et al.*, 1990) Concurrent validity data has been reported in a number of studies for example : psychiatric patients (Bramley, Easton, Morley and Snaith, 1988) , patients with a physical illness (Aylard, Gooding and McKenna, 1987) and breast cancer patients (Watson, Greer, Rowden *et al.*, 1991). The value of the instrument for use as a screening instrument in the cancer patient population has been confirmed (Razavi, Delvaux, Farvacques *et al.*, 1990 ; Hopwood, Howell and Maguire, 1991).

5.10 Pilot Work

5.10.1 Introduction

Before commencing the main study it was necessary to pre-test the individual data collection instruments and perform a small pilot study. Pre-testing explored the feasibility, accuracy, adequacy, acceptability and effectiveness of each individual instrument. The small scale administration of all the instruments and procedures explored the feasibility of their proposed scheduling, encouraged the researcher's reflection upon the proposed design, and examined practical considerations associated with the data collection strategy, sample accrual and proposed analysis. It was envisaged that this would result in the revision, clarification and development of the proposed instruments, and the modification of the design, technique and timing of administration.

5.10.2 Pre-testing

Each instrument was completed by five subjects. Patients about to receive or having received chemotherapy in the previous few weeks were approached to facilitate rapid recruitment at this early stage.

During preliminary pre-testing a number of pertinent issues were raised by the subjects concerned with understanding the instructions and items. Most related to the Piper Fatigue Scale, an instrument developed by an American nurse researcher. The other instruments were British in origin or had been subjected to extensive feasibility testing in a previous study carried out by the researcher (Richardson, 1989).

5.10.2.1 Piper Fatigue Scale

A number of issues arose during the pre-test phase. Some subjects were concerned about the instruction to place a vertical mark on the horizontal line at the *exact* spot which best indicated the degree to which they were experiencing that particular activity or how they felt/were feeling. Such precise directions were considered inhibitive. As a result it was decided to adopt the directions accompanying the HSDS, which required subjects to place a mark "At the point which most closely resembled" the degree to which they experienced the activity or feeling that day.

Several descriptors of fatigue associated with the temporal dimension were expressed by one articulate subject as possibly not meaningful to the general public. The terms "intermittent" and "continuous" were replaced by the terms "occasionally" and "all the time" in item four, and the terms "short-term" and "long-term" were substituted for the words "acute" and "chronic", in item five.

Several items comprising the affective dimension, reflecting the emotional meaning of fatigue to subjects completing the instrument were considered by the researcher and subjects alike to be difficult to interpret. After discussion and much thought, item twenty-one, where the descriptors were "protective versus destructive", were altered to read "beneficial versus harmful". In addition, the researcher questioned the use of a visual analogue scale to elicit such information . Fatigue may be viewed as categorically either unpleasant or pleasant and it would prove difficult to respond on a continuum, as required by this instrument.

Time required for completion of the instrument ranged between twenty-five minutes to one hour. This was considered too lengthy by some subjects, a view shared by the researcher; Piper (Personal Communication, 1992) reports averages of between ten to seventeen minutes to complete the original instrument. It had previously only been used to determine patients' fatigue on one or two occasions during the course of chemotherapy. Consideration needed to be given to the potential unsuitability of the instrument for eliciting information on a regular basis with only short periods between each administration .

Implicit within the scale was an assumption that the subject would be fatigued to some extent. Items contained in the temporal dimension (particularly three, four, five, six and seven) did not allow a response indicating that the person was not fatigued. Items within the affective dimension, (nineteen, twenty, twenty-one, twenty -two and twenty-three) also posed this problem, the respondent being obliged to respond to the prompt "To what degree would you describe the fatigue which you are experiencing now as being ...". Piper provides instructions to the form responses should take if not fatigued: subjects are instructed at the beginning of the instrument to describe how they felt today. It was assumed by the present researcher that the respondent would place a vertical mark at the furthest left hand side of the 100 mm line, giving a value of zero to be added to any cumulative score, otherwise an unacceptable number of missing items would result.

The points raised above, concerned with difficulties encountered by subjects when completing the instrument, led the researcher to review again, in detail, the original article describing instrument development (Piper, Lindsey, Dodd *et al.*, 1989) .

Close scrutiny revealed that many subjects refused to participate (n=47) resulting in data being collected from only fifty subjects. Reasons volunteered often constituted "Not wanting to think about the disease any more than I already have to". Of the fifty subjects who attempted to complete the instrument twelve (24%) experienced difficulties in responding to visual analogue scales. Marking lines at the extreme end points, writing in word responses and placing a 'x' and a check mark were described by Piper as some of the difficulties encountered. These twelve subjects frequently omitted items. Eight subjects who left more than 9% of the questions unanswered and also encountered difficulties were not included in the final analysis.

There was no further discussion of attempts to probe other possible reasons for difficulty or non completion of items. This is disappointing at this early stage of instrument development - and leads to questioning of the rigour employed during construction and testing. In the pilot study conducted for the present research, reasons for missing items were vigorously pursued and as discussed above, a number of patients were unsure of how to respond if they were not experiencing fatigue. In addition, item sixteen, which related to the influence of fatigue on sexual activity, was not completed by two respondents. Reasons given were that one subject was a widower and the other had recently undergone a hysterectomy : thus they were unable to estimate the particular effects of fatigue on this activity. Moreover the subject who had recently undergone a hysterectomy felt she could not respond to item nine concerned with housework. She had been advised not to take part in this activity at present.

The issue of how to handle missed items during analysis had been partially answered by Piper (Personal Communication, 1992). She suggested that these be dealt with utilising mean item substitution in each subscale, providing the majority of items have been completed. It was concerning that Piper reported that only eighteen subjects completed all four subscales on the PFS to permit calculation of a total score.

However, this disclosure did not resolve the difficulty of how to handle the data when subjects failed to complete the majority of items in a section, when they are not experiencing fatigue, or did not understand the nature of the question. Instructions for researchers accompanying the instrument suggested that if only a few items on each subscale were omitted but subjects answered the majority of individual subscale items (i.e. 75% or more), mean item substitution should be utilised to calculate the missing value(s) for the item(s).

It appeared that Piper did not encounter as many problems during the process of instrument development, or, through a lack of investigation into the reasons for non-completion of items, failed to appreciate these significant aspects concerned with the instrument's reliability, validity and usability.

5.10.2.2 Diary

Four out of five subjects completed the diary for a period of one month. The fifth subject was rapidly re-admitted to hospital due to ill health and therefore did not complete the diary.

The tasks involved in diary completion were quickly grasped. Sometimes subjects said that they found the diary repetitive and boring, feeling it produced similar information continuously. However, this was counterbalanced by the fact that subjects felt they did not have to summon up a great deal of motivation to complete the relatively quick and easy task. It could be argued that subjects may have been less precise in their responses than would be desirable. On visual inspection of the responses it appeared that there was variability in the extent and severity of fatigue and the degree of associated distress. Occasionally subjects completed the diary the following day, because they were too tired or had simply forgotten. They did not perceive this to be detrimental, feeling able to recall their responses accurately. Items eliciting the severity of fatigue and the extent of fatigue produced difficulties for subjects when attempting to discriminate their responses to these individual items. The difference between the two is considered a subtle and important difference, differentiating and quantitatively expressing how much fatigue the subject had experienced on the day in the first question, in contrast to how bad it was in relation to previous experiences with fatigue in the second question. A decision was made only to include the item reflecting the extent of fatigue that was experienced in the revised version as it was a difference that subjects did not appreciate without repeated and exhaustive explanation.

A structural change was incorporated. Due to the allocation of two lines to subjects for recording a behaviour which they initiated to help cope with fatigue, they often cited two separate behaviours but could only respond to the perceived effectiveness and source of idea for one of them. On analysis it would not be possible to estimate the perceived effectiveness/source of idea for each separate behaviour. One line only was now allocated to force respondents to record such information for each behaviour.

The open question concerned with the perceived cause or contributory factors to fatigue was altered to reflect the possibility that the subject might not have experienced fatigue that day i.e. "If you felt tired, what do you believe most directly contributed to or caused your fatigue?".

The question requiring subjects to record the most helpful activity/or strategy which they used that day to help relieve fatigue was deleted because this was repetitive following completion of the self-care section. An additional question to ascertain if the subject perceived whether they had experienced any other problems/symptoms that day was now included :-
"Did you experience any other problems/symptoms today?"

NO ☐
YES ☐ Please describe

5.10.2.3 Patient participation notes

The researcher became concerned about the accuracy of recording the stage of disease from the medical notes as this usually reflected the position at diagnosis rather than at data collection. The progression of the patient along a disease trajectory and the recording of the position on this trajectory to inform any description of fatigue was considered vital. To overcome this difficulty in the main study, a judgement was made jointly between the researcher and the clinical staff, and recorded by the former concerning the disease status of the patient (no disease, locally advanced disease, or metastatic disease), the intended nature of the chemotherapy (neoadjuvant, adjuvant, for metastatic or locally advanced disease) and whether therapy was intended as palliative or non-palliative treatment. In addition, the presence or absence of liver metastases was considered a further variable that might influence fatigue.

5.10.3 Issues arising from pre-testing

The issue of obtaining an accurate description of the fluctuations in fatigue and postulated associated factors over the course of chemotherapy was a matter of great concern, tempered by the worry of over-burdening respondents at a time when they might be fatigued and suffering other symptoms associated with chemotherapy. It was considered necessary to explore day to day variability and identify trends in time.

Previous work by a number of researchers had begun to identify a pattern whereby fatigue is at its worst during the first week following chemotherapy, then subsided over the rest of the course. The researcher held reservations about the reliability and accuracy of some of these findings as sample sizes were small, often there was a reliance on recall at interviews at the end of the course (Jamar, 1989) particularly as data were not always collected every day (Holland, 1991 ; Pickard-Holley, 1991) and consideration was not given to the particular course of chemotherapy received. There was a concern that the peak of fatigue might have occurred before or after the day on which the data was collected as no other measurements were recorded.

The phenomenon of fatigue may be rapidly changing in the first few days following chemotherapy. The question emerged of whether the proposed plan of data collection would document the phenomenon and its influential factors sufficiently. With these points in mind it was decided to ask ten subjects to complete the PFS daily for seven days immediately following chemotherapy to provide some information about possible important patterns occurring during this time. These data would, in combination with the data from the daily diary pre-test obtained over the period of a month, allow opportunity for reflection on the type and amount of data it was possible to obtain from subjects.

At this point it might have been considered necessary to collect more information than envisaged originally on a daily basis particularly in relation to mood and symptom distress rather than at seven-day periods. This could have led to the deletion of the instruments to record mood and symptom distress on day one, seven, fourteen and twenty-one, so as not to overburden subjects. It was envisaged that a compromise might be necessary between the brief ratings of fatigue obtained on a daily basis and the comprehensive PFS completed at seven-day intervals. Details of the compromise reached appear in the next section. The consequence of this compromise would be the development of a brief but informative daily measure of fatigue and selected postulated influencing factors.

5.10.4 Design of the pilot study

Data collection with the PFS administered for seven consecutive days following the administration of chemotherapy, failed to progress to ten subjects as planned. Four participants only were asked to complete the instrument. On visual inspection of this limited data set it was obvious that there was wide variability and fluctuation in the dimensions of fatigue during this time, but gathering a complete picture was hampered by

the continual problem of subjects not completing a number of items. Due to participants consistently experiencing difficulties in completing all of the instrument a decision was made not to collect any further data with this instrument at this point.

However, the researcher was surprised and gratified to encounter a high level of subject compliance in completing such a lengthy instrument each day, for seven days. It appeared that subjects were willing to complete a relatively large amount of material on a regular basis.

Considering the recurrent problems encountered with the PFS, as discussed previously, and the obvious fluctuations encountered in levels of fatigue during the month following chemotherapy administration, it was believed that by slightly lengthening the daily diary to include a representative number of items from some of the dimensions identified by Piper (temporal, intensity/severity, sensory, calm versus nervous, happy versus sad, able to concentrate versus unable to concentrate) and a number of items concerned with mood and symptoms (appetite, lack of sleep and nausea), a composite but not exhaustive daily picture of fatigue associated with chemotherapy would emerge. The relative importance of these items as opposed to the selection of alternatives was grounded in the responses derived in the pre-testing phase of the study, the literature, and clinical intuition.

The diary for the pilot study comprised two sections. Section A would only be completed if the participant had felt fatigued that day and included items concerned with:

- The extent of fatigue experienced
- The degree of distress associated with fatigue
- The degree to which fatigue interfered with ability to carry out daily activities/chores
- The degree to which fatigue interfered with doing things the participant particularly enjoys
- An indication as to the time(s) of day when fatigue occurred
- Actions taken to relieve fatigue, perceived effectiveness and source of idea for the named action
- The perceived cause(s) or contributory factor(s) associated with fatigue.

Section B was completed by all respondents and comprised six visual analogue scales concerned with aspects of mood and symptom distress, and an open ended item to document any other symptoms/problems encountered that day. This was completed on a daily basis for a period of one month.

The use of the former previously developed instruments to measure mood (MACL) and symptom distress (HSDS) on a daily basis was considered to be neither practical or desirable and these were completed at seven-day intervals, as an integral part of the diary. Participants did not complete part B of the diary on these occasions as the material was to a certain degree repetitive.

Increasing the length of the diary slightly and including items expected to vary on a day to day basis would also combat some of the repetition/boredom encountered by subjects when completing the original pre-test diary .

Informed by the literature, a decision was made to initiate telephone contact with the subject fourty-eight to seventy-two hours after returning home, if this was agreeable to them, whilst they were in the process of completing the diary. This would have the purpose of clarifying any points and addressing any worries they might encounter when completing the instrument. Participants who visited the oncology unit during the course of chemotherapy, for example for a check blood count, would be contacted at these times to monitor progress. The usefulness of these procedures in maintaining the sample would be evaluated by discussion with the participants when they returned the diary.

The issues surrounding the PFS and its utility in its present form every seven days have been discussed above. A number of refinements were incorporated into the tool, to give subjects the best possible chance of completing it without radically altering its structure or content (see Appendix J).

It was planned to administer the instrument once only, at the end of the data collection period, following a parting interview. This would produce a large amount of cross-sectional data in relationship to fatigue in a British population of chemotherapy patients, and allow further testing of aspects of reliability and validity considered to be crucial.

The refinements included:

- Adaptation of directions for completion utilised in the HSDS.

- Substitution of a number of the terms utilised in the temporal dimension.

- Instruction on the nature of response to the items if the subject was not fatigued (i.e. to describe how they felt that day), would be highlighted and the subject's attention drawn to this when they were shown how to complete the instrument.

5.10.4.1 The role and timing of the interview

During the pre-testing phase the researcher was concerned that significant information was absent, inherent in the nature of the data collection instruments selected, particularly in relationship to some baseline data e.g. concurrent illness, support at home and employment pattern. These variables are postulated to exert some influence on fatigue. In addition, preliminary information concerned with previous experiences of fatigue would be beneficial and opportunity could be taken to ascertain if fatigue and tiredness were perceived to be synonymous. To obtain this data a decision was made to formulate a preliminary interview (Appendix K) for inclusion in the pilot study, which would focus on four areas:

- Health status, taking particular note of any concurrent illness

- Ability to manage at home, taking particular note of domestic responsibilities and any provision for support

- Employment, determining whether the participant worked or usually worked at present

- Fatigue, exploring whether the participant had felt fatigued recently, what they perceived to account for this/be related to this (e.g. disease, treatment, symptoms, demands of home and work), expectation of fatigue, differentiation between fatigue experienced at present and fatigue experienced prior to present illness and some important temporal aspects. In addition, subjects would be asked their opinion as to whether they felt fatigue and tiredness to constitute similar or different feelings

This interview was semi-structured but informal, and provided an opportunity for the researcher to form a relationship with the participant.

To complement this information a parting interview was conducted to determine if there had been any significant changes in the participant's life during the period of data collection, particularly in relation to health status, household responsibilities/support, employment and aspects of fatigue (Appendix L). It also ascertained whether the participant could identify any means by which health care professionals could assist subjects to cope with any fatigue they had experienced.

During the pilot study an important feature of the parting interview was to discuss with the participant any problems they felt they had experienced filling in the diary and their perceptions concerned with repetition, boredom and ease of completion.

5.10.5 Conduct of the pilot study

Utilising a sample of ten patients a small scale pilot study involving the administration of instruments and evaluation of the feasibility of procedures was carried out (see figure 5.5). Its aim was to reveal areas which required revision, clarification and adjustment, and to develop a smooth technique for administration, considering that the instruments would previously have been presented individually to the participants (as in the pre-test), rather than in combination.

5.10.6 Results of the pilot study - final revision of the design

All ten diaries were returned. However, one was not suitable for analysis because the subject omitted a large number of items despite repeated explanations on how to complete a visual analogue scale. A number of minor amendments were made as a result of slight problems transpiring during the pilot study.

Figure 5.5 Procedure adopted for the pilot study data collection

1. Introduction to potentially eligible participant by one of the oncology sisters to explain the purpose of the study and what participation would involve, including the amount of time required. This was followed by explanation and review of the diary, pointing out the instructions on the front and the styles of completion for the different instruments.

2. Obtain agreement to participate and signing of consent form.

3. An introductory interview.

4. Participants were are asked to complete Holmes Symptom Distress Scale, Mood Adjective Checklist and day 1 of the diary. This may have been left with the participant and the researcher returned later to detect any problems with completion and to provide further clarification if necessary.

5. The diary was left with the participant and enquiries made if they were willing to be telephoned at home (2-3 days following return home) to ascertain if they had any queries concerned with completion of the diary.

6. Completion of patient participation variables from the case notes with queries to nurse or doctor.

7. Participants were phoned at home to ascertain if they had any questions. Some patients remained in hospital for 3-5 days, in which case they were visited and diary completion reviewed.

8. In the event of the participant visiting the oncology department or clinic during the month of data collection for example for a blood test or chemotherapy bag change in those having continuous infusions every effort was made to make contact and review progress with diary completion. Participants were rung again if they wished, and again on the day prior return, to remind them to bring the diary.

9. On return to hospital for next the course of chemotherapy the researcher met with the participant, completed the parting interview and asked whether the participant would be willing to complete the Piper Fatigue Scale.

10. Thanked for participation.

The patient participation notes used to record biographical and other pertinent information related to treatment patterns proved to be adequate. The diary in the main had proved usable. However , on reflection, taking into consideration that a number of subjects had failed to complete the latter half of the items concerned with other symptoms, it appeared logical to reverse the order of section A and section B. Hence participants were now asked to complete the items concerned with feelings and selected symptoms first, as this was relevant to them all. Those who had experienced fatigue on that day were invited to go on to section B dealing with the fatigue they had experienced and the performance of associated self-care behaviours. Instructions at the front of the diary and accompanying each day were altered to reflect this , and explained that subjects would be asked how they felt in general , and about the possible experience of fatigue. The item concerned with the occurrence of other symptoms and problems experienced that day was shifted to appear in the latter section , as this information was relevant only if the subject had experienced fatigue. Consistency in using the word "fatigue" rather than "tiredness" was checked so that subjects interpreting these words as not synonymous were not confused and responded consistently.

Within the preliminary interview it soon became apparent that the question concerned with asking the subject whether they differentiated between the terms "fatigue" and "tiredness" should feature at the beginning of questioning. This would clarify subjects' frame of reference when responding to further items, for example, those concerned with their opinions concerning any contributory factors associated with fatigue.

Participants all considered the telephone calls to be helpful. They often took the opportunity to seek further clarification and reassurance that they were completing the diary correctly and valued the contact with the researcher.

On examining the completed MACL, and in conversation with subjects, it became apparent that owing to the manner in which the items were ordered, a number had responded in a fixed manner. They had assumed that all the items in the instrument reflected negative feelings and marked every box accordingly. The order of the items had been randomly generated in Wilson-Barnett's (1977) study, when this problem had not been encountered. There are, however, a far greater number of negative feelings compared to positive ones , so any process of random generation would not overcome this. A decision was made to place one positive item , in this case the adjective "vigorous" , near the top of the checklist.

Consideration was given to preparing a number of versions of the MACL and the HSDS , suitable for use on repeated occasions. This strategy was rejected for two reasons; firstly, a period of seven days transpired between each completion and secondly the previously completed instruments were bound together in the diary, so subjects could compare their present response to previous responses.

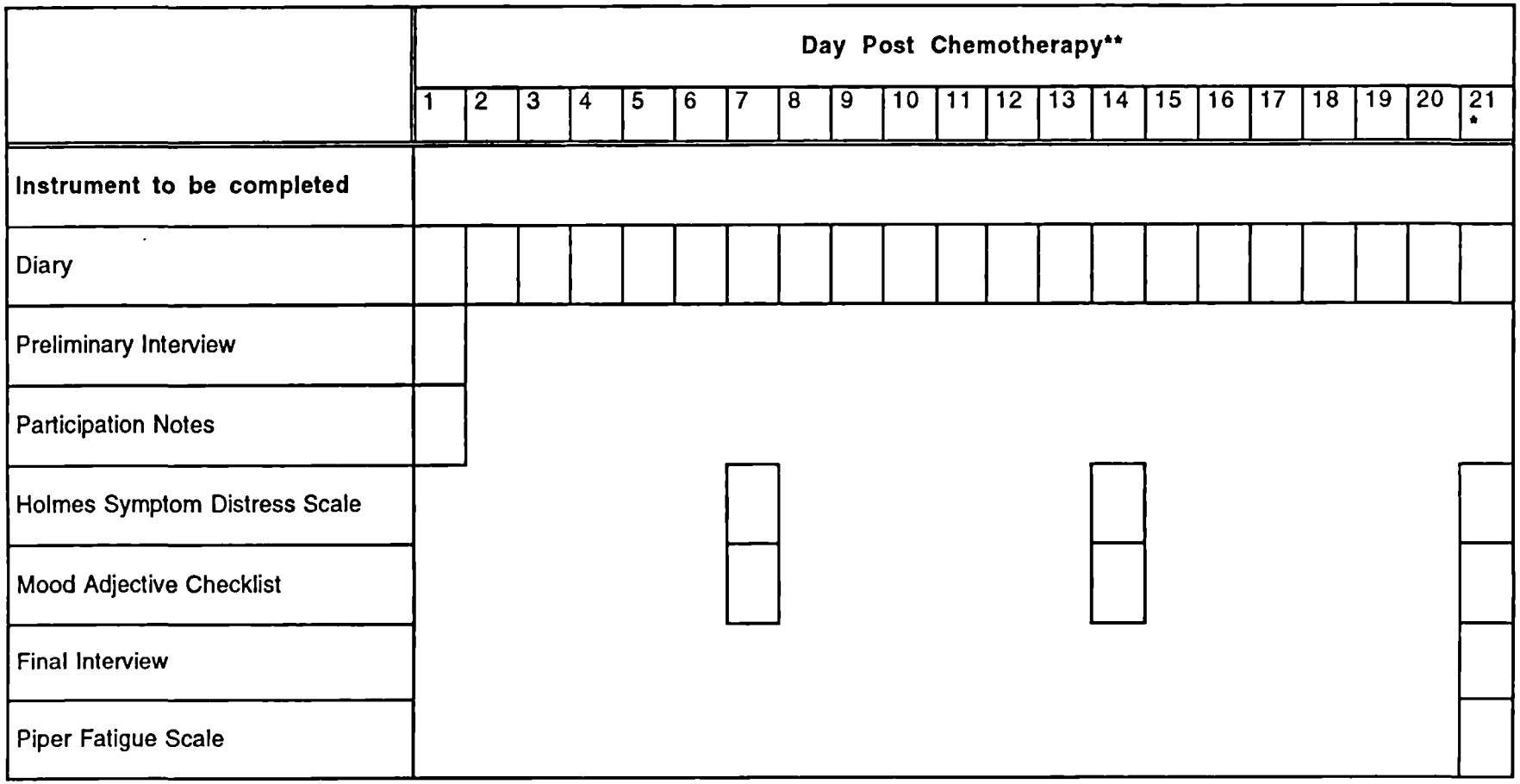
Scheduling completion of the MACL and the HSDS on the day of chemotherapy proved not to be feasible. Obtaining consent following explanation of the study, taking part in the interview and illustrating how to complete the diary often took up to an hour and a half, and it was not considered acceptable to ask subjects to give this amount of time. The revised scheduling of the instruments for the main study is illustrated in figure 5.6.

The system for identifying appropriate subjects to be approached for inclusion in the study appeared to be highly successful, no doubt in part due to the enthusiasm and diligence of the staff working in the oncology unit.

The least successful attempts in completing the data collection instruments occurred in the out-patient setting. On reflection it was felt that this environment was not always conducive to correct completion of the instruments, and in future the patients would be approached on the oncology unit.

A suggestion to bind the diary in seven-day blocks had been received, with the intention of asking the subjects to return each block by post at the relevant time. This would facilitate early preliminary analysis of some of the data and identify any problems in completion. On consideration this idea was rejected as subjects would have to make a trip to a posting box specially to return the diary at the appropriate time, when they might be feeling nauseous or indeed suffering from fatigue.

Figure 5.6 Proposed data collection procedure adopted following the pilot study



* This assumes a 21 days cycle of chemotherapy, data collection extends for those subjects receiving chemotherapy based on a 28 day cycle, at which point the final interview and Piper Fatigue Scale would be completed.

** Day 1 is the day the patient receives chemotherapy.

5.11 Data Collection For The Main Study

Owing to the continuous nature of data collection, it was necessary for the researcher or assistant to be available each weekday at the site of data collection. A strategy was developed to assist with the most efficient use of time and the recruitment of the intended sample. Potential recruits were identified at the beginning of each week with the help of the oncology sisters. This technique became refined and highly co-ordinated over the period of data collection. A diary was prepared with the names of potential participants, names of any participants returning to hand in diaries and participants who required telephoning. To monitor the status of incoming data, a detailed record was continually updated (see figure 5.7). In addition, to the above activities the in-patient bed allocation was checked every few days to ascertain if any participants had been admitted, for example, due to leucopenia.

An issue of concern was whether or not the same person should meet with the participant across all data collection points or if a different person could be used. The former strategy was selected when at all possible supported by the clinical impression that the subject needed to have contact with the same person to encourage continued participation.

From the pilot study, a procedure compatible with the day to day running of the unit had been developed. The ordering of obtaining informed consent and informing subjects about the study was not changed as it was considered successful. As before, the instruments were bound together in sequential order, in an attractive package to encourage completion on the appropriate day. Following the receipt of fifteen diaries, a small addition was made to the instructions accompanying day seven, fourteen, twenty-one and twenty-eight to make clear that the subject should complete both the diary, HSDS and the MACL that day. This was done as a couple of patients had incorrectly completed the diary on these days, completing the instruments on sequential days.

Obtaining consent, providing detailed information about the study and data collection occurred either in the chemotherapy suite waiting area, or at the patient's bed-side if chemotherapy necessitated hospitalisation. Collecting data in the outpatient area was abandoned for reasons already given.

Five months into the data collection there arrived a point at which the patients available for recruitment were all just commencing course one of their chemotherapy, due to the researcher and her assistant having successfully recruited all other available

Figure 5.7 Data monitoring sheet

Subject Number	Subject Name	Date Recruited	Phone Number	Telephone 1	Telephone 2	Dates of Scans/Blood	Date Expected Return	Diary Returned	Interview Completed	Piper Completed	Comments
1											
2											
3											
4											
5											
6											
7											
8											
9											
10											
11											
12											
13											
14											
15											

patients. A recognised feature of longitudinal research is that the type of participants needed are not all available at once (Barnard, Magyary, Booth and Eyres, 1987). The researcher decided to suspend data collection at this point for a period of three to four months. Hence at recommencement of data collection patients would be receiving various of pulses of chemotherapy. Strategic sampling took place to some extent at this stage of data collection to maximise the size of the sample. The researcher actively sought to recruit subjects to the diagnostic groups which appeared robust, whilst maintaining variety in the type of tumour, chemotherapy treatment and subjects receiving different pulses of chemotherapy.

Despite the mechanisms for reminding the patients to bring their diary with them on the appropriate day, a small number did forget. When this occurred arrangements were made with the patient concerned for them to drop it in at the unit at an appropriate time or to bring it with them when they next received chemotherapy, whichever was easiest for them.

Following the receipt and review of twenty-one PFS's and thirty-four subjects had been recruited, a decision was made to abandon the use of this instrument. The researcher substituted the HADS for the PFS. There were no equivalent or similar scales concerned with fatigue that would produce useful information and it was felt the inclusion of the HADS would provide a useful albeit limited comparison with the MACL.

Thus the plan for data collection required a flexible approach responding to occurrences on an almost daily basis, but aided considerably by the diligence and helpfulness of the oncology unit and ward staff.

5.12 Data Analysis

5.12.1 Preparation of the data

Coding frames (an example is located in Appendix M) were developed and refined which listed each variable, the columns in the worksheet into which each variable was entered, and the codes and scores associated with the various aspects or attributes of the variable. Any decisions made about coding, recoding and item reversals were recorded in full, made necessary by the fact that more than one person took part in the coding activities. Data summary sheets containing the coded data (the transformed raw data in a standardised form) were prepared. These facilitated data entry onto the computer worksheets (figure 5.8 contains an example).

PAGES 181-188 ARE MISSING IN

THE ORIGINAL THESIS

CHAPTER 6

RESULTS I

6.1 Introduction

The results of the study will be presented in three consecutive chapters. Chapter 6 opens by describing the type of data collected, including the response rate and a summary of the properties of the sample. The pattern of change in fatigue is described using a number of different approaches including vignettes and individual time plots displayed to provide examples of the experiences of individual subjects, followed by a summary of the patterns relating to fatigue which emerge from visual analysis of the daily data derived from the diary. Finally, the results of a number of time series analyses are presented. These provide a statistical summary of the visual data. To aid clarity, when reporting the summary statistics percentages and other scores have been rounded to one decimal place, and p values and error rates are reported to the second decimal place. Variable labels have been italicised throughout the text of the chapters dealing with the results of the study for ease of identification.

6.2 Response Rate

Inadequate accrual and attrition of subjects pose a serious threat to the validity of findings from any research study. A number of practical strategies were used to minimise these threats and were described in the preceding chapter. One hundred and sixty nine patients were eligible to take part in the study. Patients were ineligible if they had taken part in the pilot study (n = 21) or failed to meet the inclusion criteria. The main reasons for exclusion were having a current psychiatric condition necessitating treatment (4 patients), or lack of verbal and written English comprehension (2 patients). Twenty-three patients were not interviewed for the following reasons. Three patients were missed due to the commitments of the researcher or research assistant at the time data collection was planned. Seventeen patients could not be approached because they had died, altered treatment to an ineligible group, terminated treatment early or the doctor or nurse denied permission to approach the patient. The primary reasons for nurse/doctor refusal on behalf of the patient were due to a patient's particularly stressful encounter with

treatment, physically or psychologically. This number was reduced by following up patients to see if their condition improved.

One hundred and forty-six patients were interviewed to inform them of the study and request consent. Seventeen patients refused chiefly because they did not wish to involve themselves with additional commitments of a stressful nature or because they wished to avoid involvement in any research project. Patients were not pressed if a reason was not volunteered.

Accrual to the study was possible for 129 eligible subjects for whom consent was obtained during the study period. One hundred and nine subjects commenced diary keeping. Sixteen subjects returned the diary blank or never returned it and were deemed to have withdrawn from the study. A number of subjects wrote short letters to explain why they felt they had been unable to complete the data collection. Attrition occurred due to a variety of reasons. Five subjects died during the period of data collection and 4 of these diaries were not recovered. Major toxicity resulting in a period of hospitalisation or physical and/or mental deterioration which made it difficult for the subject to continue completing the diary resulted in the withdrawal of thirteen subjects at various time points (range 1–23 days). Their data were included in the data set. Nine subjects withdrew following consent after completing the diary for a variable number of days (range 2–16 days), and these data were also included in the data set.

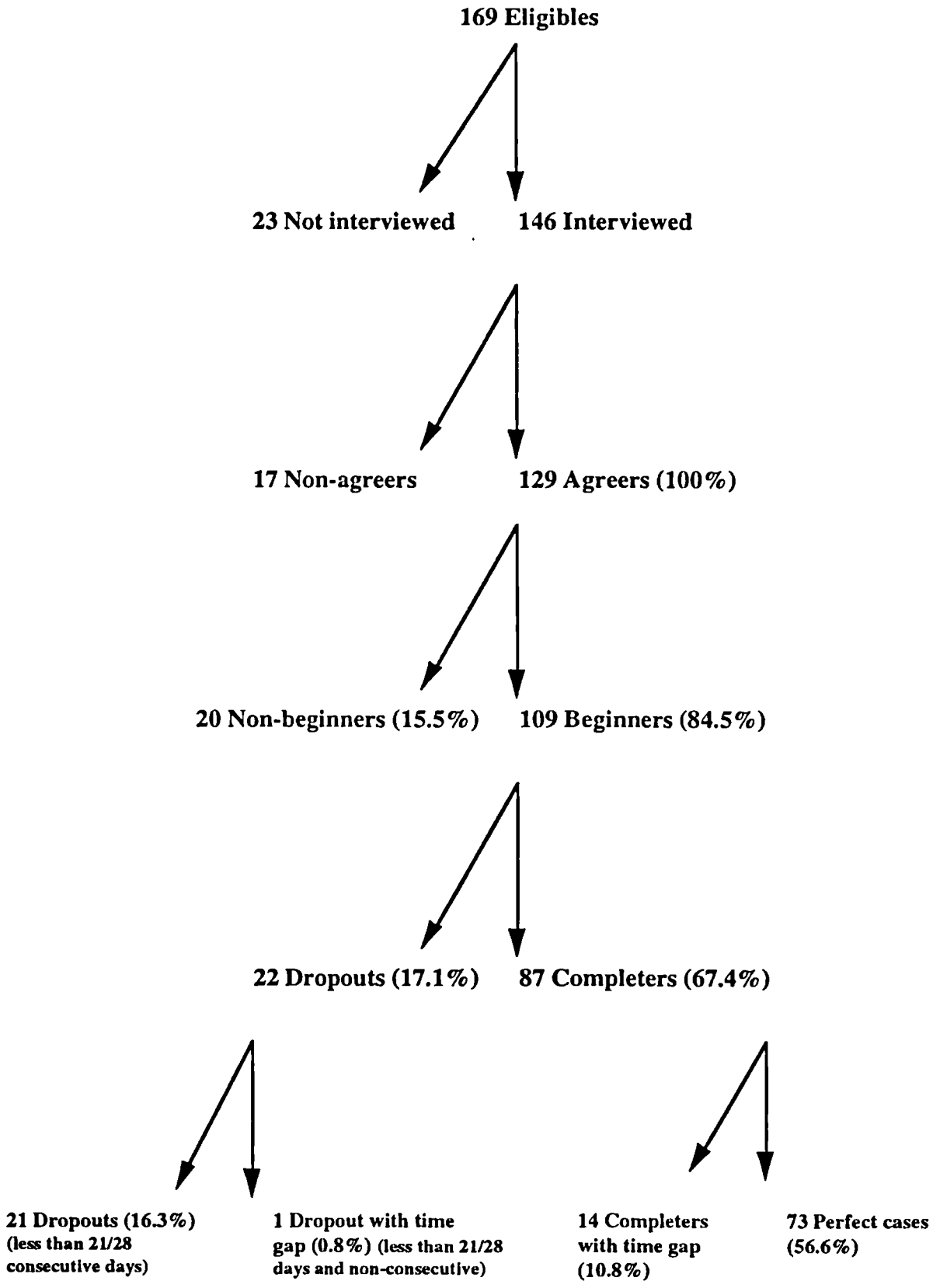
6.3 Quality Of Data

Partially or totally missing data due to attrition, as mentioned above, jeopardise the validity of any investigation. Subjects who dropped out of the study may have differed from those who wished to remain with respect to the key study variables. This section will examine the completeness and quality of data and the impact of subject attrition.

6.3.1 Diary

Table 6.1 documents the proportion of diary days completed by the sample. A continuous sequence of data were achieved by 73 participants (56.6% of the original sample of 129). These were classed as "perfect" cases. A broken sequence of data for participants who completed the diary data collection period occurred in 14 cases (10.8%).

Figure 6.1 Identification of groups that dropped out at different points in the study



These were classed as "completers with time gaps". Twenty-two participants dropped out at some stage of diary completion. Twenty-one of these cases contained data that were continuous and only one had a time gap, and thus this series was non-consecutive. Figure 6.1 provides a summary of aspects of the response and quality of data obtained.

Table 6.1 Number of diary days per participant in the study

Length of diary keeping period (days)	Number of persons	Percentage
1–7	13	11.9
1–14	7	6.4
1 21	45	41.3
1–28	44	40.4
Total	**109**	**100.0**

There was potential to collect data on 2,625 diary days from the 109 beginners. Data were collected on 2,263 diary days. Days were lost due to several reasons due to incorrect completion or to the reasons detailed above. A very small number of missing values were also present in a certain number of cases in the 2,263 diary days.

Of the 101 participants who took part in the final interview 96 subjects considered the diary keeping activity to be straightforward, although 45 subjects perceived it to be somewhat repetitive. The majority reported that they had completed the diary in the evening (87 subjects), occasionally leaving it to the next day if it was not convenient. A small number insisted on completing it the next day or retrospectively (14 subjects). The data set of each alternative participant was checked for accuracy of data entry, yielding a .01% error rate.

6.3.2 Interviews - preliminary and final

A preliminary interview was conducted for all participants. The data set of every fifth participant was checked and no errors were detected. There were 6 missing items where the researcher had forgotten to ask the pertinent question. One hundred and one final interviews were conducted. In cases where participants were not available this was due to physical or mental ill health, death or an indication that the participant did not want to participate further. The data set of every fifth participant was checked and there was a .34% error rate. There were 5 missing items where the researcher had forgotten to ask the pertinent question.

6.3.3 Hospital Anxiety and Depression Scale

Following the decision to include the Hospital Anxiety and Depression Scale (HADS) some time into data collection, 38 participants completed the scale at the time of the final interview. Only one participant declined. There were no missing data . The data set of every fifth participant was checked and no errors were detected.

6.3.4 Mood Adjective Checklist

There was potential to complete the Mood Adjective Checklist (MACL) on 375 separate occasions, but in reality it was completed 293 times (78.1%). Incorrect completion was the reason on 12 occasions (3.2%) and the fact that the subject had withdrawn on 52 occasions (13.9%) or omitted when they were particularly unwell on 5 occasions (1.3%). Opportunities were lost when the subject received chemotherapy early, this was the case on 12 occasions (3.2%) and when a subject died, on 1 occasion. Value to value verification was undertaken with this instrument as the researcher felt less convinced that the data were robust. There was a .16% error rate. Thirteen missing items were evident when an attempt was made to complete the instrument. Mean item substitution was possible with this instrument and was undertaken when 75% or more of items within a domain were completed.

6.3.5 Holmes Symptom Distress Scale

There was potential to complete the Holmes Symptom Distress Scale (HSDS) on 375 separate occasions, but in reality it was completed 301 times (80.3%). Incorrect completion was the reason on 6 occasions (1.6%) and the fact that the subject had withdrawn on 51 occasions (13.6%) or omitted when they were particularly unwell on 4 occasions (1.1%). Opportunities were lost when the subject received chemotherapy early, this was the case on 12 occasions (3.2%) and when a subject died, on 1 occasion. Every fifth data set was checked and no mistakes in data entry were evident. Fourteen missing items were evident when an attempt was made to complete the instrument.

6.3.6 Piper Fatigue Scale

Subjects who had completed diary keeping were offered the chance to complete the Piper Fatigue Scale (PFS) to further assess this instrument following the problems encountered in the pilot phase (see Chapter 5). The first 21 subjects were approached to complete this instrument, but of these only 2 managed to complete all the items on the questionnaire. After the recruitment of subject 21 it was not felt beneficial to the study to ask any further subjects to complete this instrument.

Piper, Lindsey, Dodd *et al.* (1989) omitted subjects from analysis if they failed to complete more than 91% of the VASs. When this procedure was adopted only 5 questionnaires (23.8%) were available for analysis. Of these, only 4 questionnaires contained completed sub-scales, which is necessary to compute a *total fatigue score.* In the original sample of 21 the percentage of questions answered within each subscale was as follows: *temporal* 61.9%, *intensity* 72.2%, *affective* 21% and *sensory* 82.5%.

6.3.7 Factors influencing diary completion

To analyse the present data set in which attrition had occurred, the assumption that non-respondents did not differ significantly from respondents needed to be met. Some statistical techniques were used to determine whether the remaining sample differed from the initial sample on a number of key characteristics. The Mann-Whitney or Kruskal-Wallis test statistic were used to determine if there were any factors which appeared to influence an individual's ability to complete the diary. Data were examined from the perspective of the percentage of diary days the 109 participants managed to complete and demographic and social variables of the sample. No statistically significant differences were revealed relating to the following variables :- *sex*, *age*, *diagnosis*, *type of chemotherapy*, *disease status*, *pulse*, *previous chemotherapy*, *previous other treatment*, *presence of liver metastases*, *nature of administration*, *purpose of chemotherapy*, *intended outcome*, *concurrent health problems and the severity of these*, *presence of others in the home*, *ability to manage independently at home* and *particular demands on energy*, *change in health status* during this course of chemotherapy. However, there was a significant relationship between worsening fatigue over the diary period and a lower percentage of the diary being completed : $U = 777$, $p < .05$ (one-tailed test).

To determine whether there were any differences between those subjects who agreed to keep the diary but did not commence diary keeping (non-beginners) and those who started (beginners), and between completers and dropouts, demographic and social variables were examined using the chi-square test. No statistically significant differences were revealed.

6.4 The Sample

A description of the sample is presented in table 6.2. The sample (n=129) contained marginally more females (72, 55.8%) than males (57, 44.2%). They were predominately in their fifties ($\bar{x}$ = 58 years, standard deviation (SD) = 12, range 26–82). The most common diagnosis was ovarian cancer (26, 20.2%), followed by colorectal cancer (20, 15.5%), small cell lung cancer (19, 14.8%), or cancer of the stomach, duodenum or oesophagus (17, 13.2%). The smallest group were women with a diagnosis of cancer of the cervix (2, 1.6%). Most had only been diagnosed with cancer during the previous 3 months (54, 41.9%), had metastatic disease (74, 57.4%), but had no liver metastases (98, 76%). Thus for most subjects the intended outcome of chemotherapy administration was palliation (77, 59.7%).

The subjects received one of 13 different chemotherapy protocols. The most common was the ECF combination (26, 20.2%) or single agent Carboplatin (26, 20.2%). The most common method of administration was by bolus injection or short term infusion (83, 64.3%). Frequently subjects had not received any other previous chemotherapy treatment prior to this current protocol (112, 86.8%), nor had they received any other treatment (radiotherapy, surgery or endocrine therapy (74, 57.4%). If they had received another treatment modality it was most likely to have been surgery within the previous 6 months.

Over a third (49, 38%) of the participants had an additional health problem besides cancer but this was perceived to be mild. Only 16.2% (21) of the sample lived alone. The majority lived with family, friends or a partner (107, 83%) and one woman lived within a religious community. Over half of the sample considered that, at the present time, they were managing independently at home (69, 53.5%), but a small percentage considered they needed help and assistance with most aspects of daily life (2, 1.6%). Approximately half of the sample did not have paid employment outside the home (62, 48.06%), but of those who did, 56.5% (35) had resigned due to their ill health (resulting in long term sickness arrangements or precipitating early retirement). The remainder worked either full (13, 21%) or on a part time/intermittent basis (14, 22.6%).

Following diary completion, subjects were asked to comment on the extent to which factors in their lives had changed over the data collection period. Most (58, 57.4%) reported that they were managing daily activities and demands to the same extent as reported in the preliminary interview. However, a number reported decreased (11, 10.9%) and increased (21, 20.8%) ability. In 11 cases subjects found it difficult to comment because they had been hospitalised prior to or during this current pulse of chemotherapy. Those subjects who were managing less well were receiving help (6) or had decided to do less (5). In 92% of cases, subjects were not receiving help from a different source than before this pulse of chemotherapy. Subjects' pattern of work on the whole had not altered (91, 90.1%). However, 6 subjects (5.5%) had resumed work on a full or part-time basis, 2 subjects (2%) were now working part-time or reduced hours, and 2 (2%) were no longer working at all.

Table 6.2 Description of the sample *n* =129 (% in brackets)

Gender	
Male	57 (44.2)
Female	72 (55.8)

Site of cancer	
Ovary	26 (20.2)
Colorectal	20 (15.5)
Small Cell Lung	19 (14.7)
Non-Hodgkin's Lymphoma	18 (14.0)
Gastric/Duodenum/ Oesophagus	17 (13.2)
Pancreas	7 (5.4)
Breast	7 (5.4)
Unknown Primary	6 (4.7)
Hodgkin's Lymphoma	4 (3.1)
Bile Duct	3 (2.3)
Cervix	2 (1.6)

Age	
20–29	3 (2.3)
30–39	7 (5.4)
40–49	18 (14)
50–59	39 (30.4)
60–69	38 (29.5)
70–79	22 (17.1)
80–89	2 (1.6)

Time since diagnosis	
0–3 months	54 (41.9)
4–6 months	43 (33.3)
7–12 months	11 (8.5)
Over 12 months ago	21 (16.3)

Disease status prior to chemotherapy	
Metastatic	74 (57.4)
Locally advanced	42 (32.6)
No disease	13 (10.1)

Treatment	
Carboplatin	26 (20.2)
Epirubicin, Cisplatin & 5-Fluorouracil (ECF)	26 (20.2)
Epirubicin & Etoposide	19 (14.8)
Cyclophosphamide, Epirubicin/Adriamycin, Vincristine & Prednisolone (CEOP/CHOP)	16 (12.4)
5 - Fluorouracil & Levamisole weekly	10 (7.8)
Cyclophosphamide, Methotrexate & 5-Fluorouracil (CMF)	7 (5.4)
Cisplatin & 5-Fluorouracil	7 (5.4)
5 - Fluorouracil weekly	7 (5.4)
Chlorambucil, Procarbazine, Vinblastine, Prednisolone (CHLVPP)	3 (2.3)
Continuous infusion of 5-Fluorouracil	3 (2.3)
Cisplatin, Methotrexate & Bleomycin (PMB)	2 (1.6)
Vincristine, Epirubicin, Etoposide & Prednisolone (VEEP)	2 (1.6)
Etoposide, Ifosfamide, Cisplatin & Prednisolone (EPIC)	2 (0.8)

Presence of Liver Metastases	
Absent	98 (76)
Present	31 (24)

Purpose of Chemotherapy	
Neo Adjuvant	10 (7.8)
Adjuvant	16 (12.4)
For Metastatic Disease	74 (57.4)
For Locally Advanced Disease	29 (22.5)

Pulse	
1	20 (15.5)
2	20 (15.5)
3	23 (17.8)
4	13 (10.1)
5	14 (10.9)
6	19 (14.7)
Not applicable	20 (15.5)

Intended Outcome of Chemotherapy	
Non-palliative	52 (40.3)
Palliative	77 (59.7)

Nature of Administration	
Bolus &/or short term infusion	83 (64.3)
Bolus & Continuous	26 (20.2)
Intermittent Bolus	17 (13.2)
Continuous	3 (2.3)

Previous Chemotherapy	
Yes	17 (13.2)
No	112 (86.8)

Previous other Treatment	
Yes	55 (42.6)
No	74 (57.4)

6.5 Perceptions Of Fatigue And Tiredness

A preliminary interview was conducted with all subjects who were enrolled in the study. The main purpose of this was to gain information about previous and current experiences of fatigue, and provide details of subjects' current health status and lifestyle. The results gained from the latter line of questioning have been outlined above when describing the nature of the sample.

The majority of the sample (67.7%, 84) did not consider tiredness and fatigue to constitute the same feelings. The dimensions of fatigue selected by Piper, Lindsey, Dodd *et al.* (1989) which were initially derived from her clinical experience and the literature concerning the conceptualisation and measurement of symptoms in general, and the symptoms of pain and fatigue in particular were used to organise the responses into themes; temporal, severity, affective, sensory and evaluative. Temporally fatigue was perceived as "more long-term" and the descriptors "chronic", "persistent" and "long lasting" were used. In terms of intensity and severity, fatigue was considered to be "more severe", "an exaggerated form of tiredness", "a more intense feeling" and associated with "absolute exhaustion". Tiredness was often perceived to be a "normal" sensation, something that was "natural" and more "healthy" than fatigue. Physical, mental and emotional sensations were attributed to fatigue and tiredness. The mental nature of fatigue was often emphasised when subjects commented it is "more mental", "it is more like boredom" and fatigue "is psychological where you can't be bothered to make too much of an effort". Subjects felt "washed out" and fatigue affected the whole body, leaving subjects feeling "absolutely exhausted and absolutely drained". Some of the participants considered tiredness and fatigue to be on a continuum, whilst others considered them to be different sensations and to be associated with differing precursors. For example :

Subject 93 "They are the same thing, but fatigue is worse in intensity. They are on the same continuum"

Subject 40 "Tiredness is more common. Fatigue is a more exaggerated form of tiredness"

Subject 67 "Tiredness is when you feel sleepy. Fatigue is when you are absolutely exhausted and absolutely drained. You feel so ill you can't sleep and can't relax"

Subject 58 "Tiredness is due to not sleeping. Fatigue is associated with overwork."

Conflicting opinions were evident in terms of how fatigue and tiredness were evaluated and in terms of whether or not they constituted mainly mental or physical feelings. However, the majority view was that tiredness was generally believed to be relieved by sleep, whereas fatigue did not resolve with sleep or rest :

Subject 66 "Tiredness is due to lack of interest or lack of mental activity. Fatigue occurs after strenuous physical activity"

Subject 120 "Tiredness is physical and short-term. Fatigue is a combination of mental and physical things, much more intense, lasts for a longer period of time and is less likely to go following sleep".

Subject 44 "With tiredness you need sleep and it is relieved by sleep. Fatigue implies you are absolutely shattered and it is not relieved by sleep".

The majority of this sample appeared to consider fatigue to meet the criteria for chronic fatigue outlined by Piper (1988), in that it was a more generalised whole body-mind sensation and not completely dispelled by such measures as adequate rest and stress management techniques. Tiredness was similar in nature to acute fatigue in that the cause was usually identifiable and related to some form of activity and exertion which would resolve rapidly with the instigation of appropriate relief measures.

6.5.1 Previous experience with fatigue

Over 85.3% (110) of the sample had found fatigue to be a problem recently, attributing it to a combination of factors : 42.3% (52) thought it was due to their illness, 78.2% (86) thought it due to the chemotherapy treatment, 31.9% (35) due to a change and/or quality of sleep pattern, 36.4% (40) due to the presence of symptoms, 23.4% (29) related it to a depressed mood, and 18.1% (20) due to the demands of home and/or work. Only one subject failed to identify the cause of their fatigue. The participants could select more than one factor and often did. A few admitted that they did not know or were not sure what they associated the fatigue with.

For the 26 subjects embarking on their first pulse of chemotherapy or prior to commencing weekly or continuous 5-Fluorouracil (5-Fu), half were expecting fatigue to be a problem during chemotherapy, and 8 remarked they were not sure or did not know.

When the sub-group of 15 subjects who considered themselves to have experienced fatigue previously were asked to reflect on the nature of the fatigue they had experienced since the onset of their illness, 7 described it as different and much worse, as oppose to the same (3), the same but increased in quantity (1), different but not worse (3) or did not know (1). They were equally divided when asked whether they considered this fatigue to be abnormal or unusual. It was considered by 8 of these subjects to occur every day, but in the main was a problem for some (8) or most of the day (6) rather than all of the day (1).

In the remaining subjects who had already commenced treatment with their current chemotherapy protocol (103), 78 were anticipating fatigue to be a problem during the period of data collection. The 95 subjects (of the sample of 103) who had experienced fatigue previously with this current chemotherapy protocol were asked to reflect on the nature of the fatigue they had experienced recently. They described it as either different and much worse (34, 35.8%) or different but not worse (32, 33.7%), rather than the same (10, 10.5%), the same but increased in quantity (12, 12.6%) or they did not know (7, 7.4%) to that compared with any fatigue they may have experienced prior to the start of chemotherapy treatment. Well over half (59, 62.1%) considered this fatigue to be abnormal or unusual in some way. It was considered by 56.8% (54) of this sub-sample to occur on some of the days, rather than most days (9, 9.5%) or every day (32, 33.7%), and when it did occur was a problem for some of the day (52, 54.7%) rather than most of the day (26, 27.4%) or all of the day (16, 16.8%,).

A Mann-Whitney test revealed a significant association between those who expected to experience fatigue and those recording a higher respondent *mean fatigue score* ($U = 284, p < .01$, one tailed test).

6.6 Pattern Of Change In Fatigue

The main aim of the study was to monitor the subjective dimensions of fatigue related to the administration of chemotherapy (including information concerned with the onset, pattern, duration, intensity and distress caused by this phenomenon), as documented by subjects in the diary. Sections 6.6.1-6.6.2 will detail the patterns of change in the daily fatigue items recorded in the diary based on a visual analysis of the data. Diary plots were created for all subjects who commenced diary keeping. The plots reproduced in figures 6.2–6.5 show the different trajectories for 4 subjects. Figure 6.6 illustrates the patterns evident in the *mean fatigue scores* when considered by *type of chemotherapy* protocol. They depict both raw and "smoothed" data. The data were complex and in order to visualise them more easily and identify trends a statistical manipulation was performed. Data were "smoothed" within the Minitab programme using the resistant smoother 4253H, twice. As explained in Chapter 5 resistant smoothers are often used on data collected in time order and are built up from successive applications of simple smoothers such as running medians. To recap, the running median replaces each data value by the median of the data value immediately before and after it. The smoother 4253H, consists of a running median of 4, then 2 , then 5, then 3, followed by Hanning (Hanning replaces yt by the running average $\frac{1}{4}yt_{-1} + \frac{1}{4}yt + \frac{1}{4}yt_{+1}$). The residuals, or rough, are then "smoothed" by the same smoother. The smooth of the residuals is then added to the smooth of the first pass to produce the full smoother, 4253H, twice.

Following the results from the visual analysis the results of a number of time series analyses are presented. This is a form of statistical analysis which is considered eminently suitable for the study of change over time enabling the generation of statistical models to explain such data. The methods used to identify and confirm the presence of a number of different models in relation to fatigue and the other variables studied on a daily basis are summarised in section 6.6.3.

6.6.1 Vignettes

A number of vignettes and their accompanying time plots generated from the recordings in subjects' diaries follow. These have been selected to illustrate different facets of change, some commonly encountered and some not, and the nature of the personal data generated through the short interviews and diary recordings. They are accompanied by summary statistics which indicate the level (mean score over diary period) and changes (fluctuations over the diary period, indicated by the range and standard deviation) in the variables over the diary period.

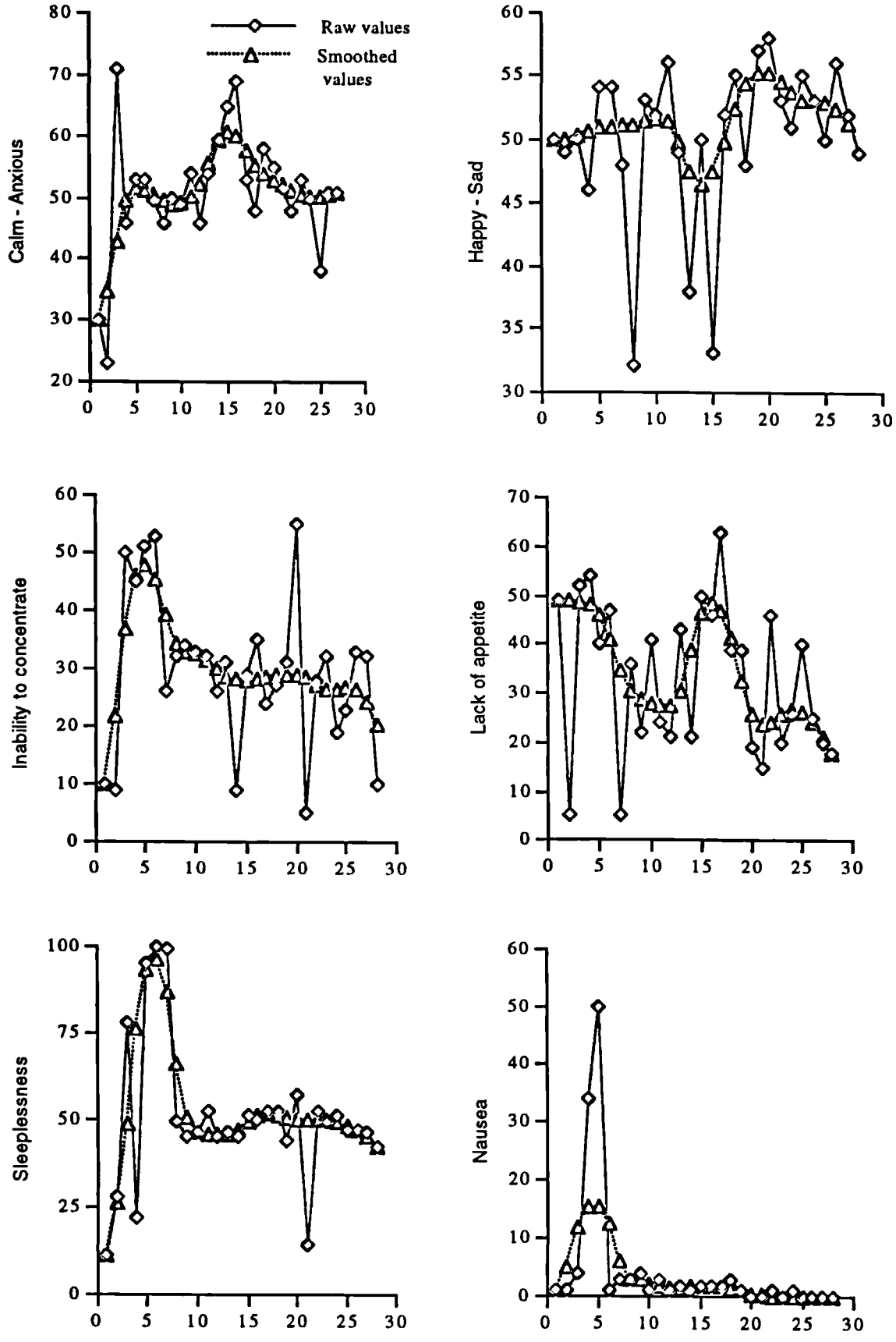
6.6.1.1 Subject 1

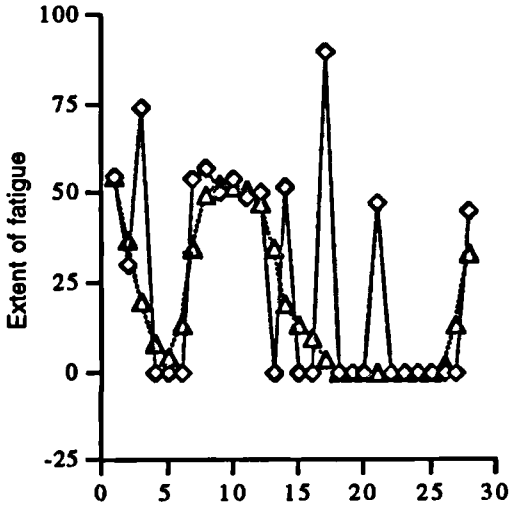
Subject 1 is a 47 year old woman with a diagnosis of metastatic breast cancer. She is receiving chemotherapy for palliative purposes as the cancer has spread to her liver. She had been diagnosed three months ago and is undergoing her third course of CMF chemotherapy. Radiotherapy and surgery had not been attempted. She is widowed with two teenage sons who help around the house with general tasks, but on the whole she copes independently with the cooking and cleaning. She has found her job in full-time kitchen work too heavy to continue since the onset of her illness. This subject considers fatigue to be a worse sensation than tiredness and one that encompasses the whole body. She has found fatigue to be a problem with the commencement of chemotherapy and attributes it to the treatment, poor sleep and the demands of looking after two teenage sons single-handed. She did not expect to feel fatigued but now expects it with every course. It occurs everyday to some extent with a worsening on day 2 of the pulse, developing in the late afternoon and early evening.

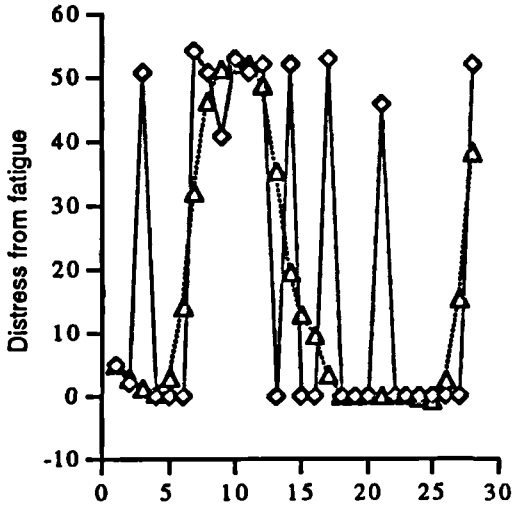
The time plots of fatigue illustrate a typical fluctuating pattern, with the *mean fatigue score* ranging from 0–82 with a $\bar{x}$ = 23.9 (SD = 28.0) and the sub-dimensions closely mirroring the *mean fatigue score.* As she had predicted, fatigue rose on day 2 and then disappeared for a number of days. Following this, fatigue exhibited a volatile pattern severe on some days, completely absent on others. The other visual analogue scales seem to represent a parallel pattern apart from *sleep* and *nausea. Nausea* was only reported as a problem in the first week. It then subsided becoming virtually absent, a common pattern in the majority of subjects. Problems with sleeping appeared to recur throughout the 28-day period except for a slight improvement on day 21.

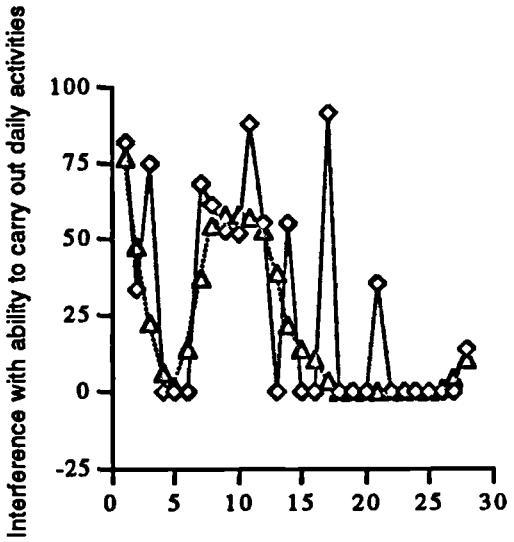
When she returned the diary to the researcher and was asked whether she had experienced any change in her health status during the past 28 days, this subject felt that she was more moody and attributed this to conflict with her sons. At home she felt she was managing more of the house. Fatigue had improved but she was unsure why, suggesting that the arrival of spring could account for it. She reflected that she had not done anything that had helped to significantly alter her fatigue. This was confirmed in the lack of recordings in the diary concerned with self-care actions except on one day when she baked a cake with her small niece.

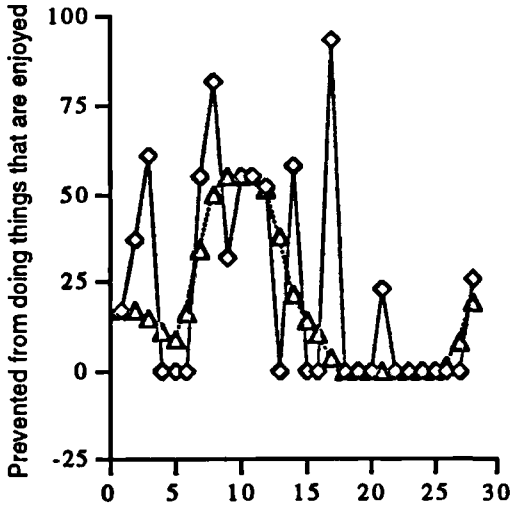
Figure 6.2 Pattern of daily diary items and summary statistics for subject 1

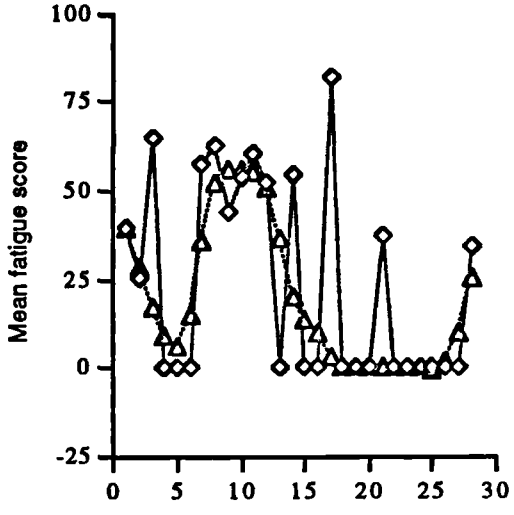












Summary statistics

Variable	Mean	SD
Calm-anxious	50.6	10.4
Happy-sad	50.1	6.4
Concentration	29.4	13.4
Appetite	33.0	15.4
Sleeplessness	50.5	21.6
Nausea	4.3	11.0
Extent	25.3	29.2
Distress	20.1	25.1
Daily activities	27.3	33.4
Hobbies	23.1	29.4
Mean FS	23.9	28.0

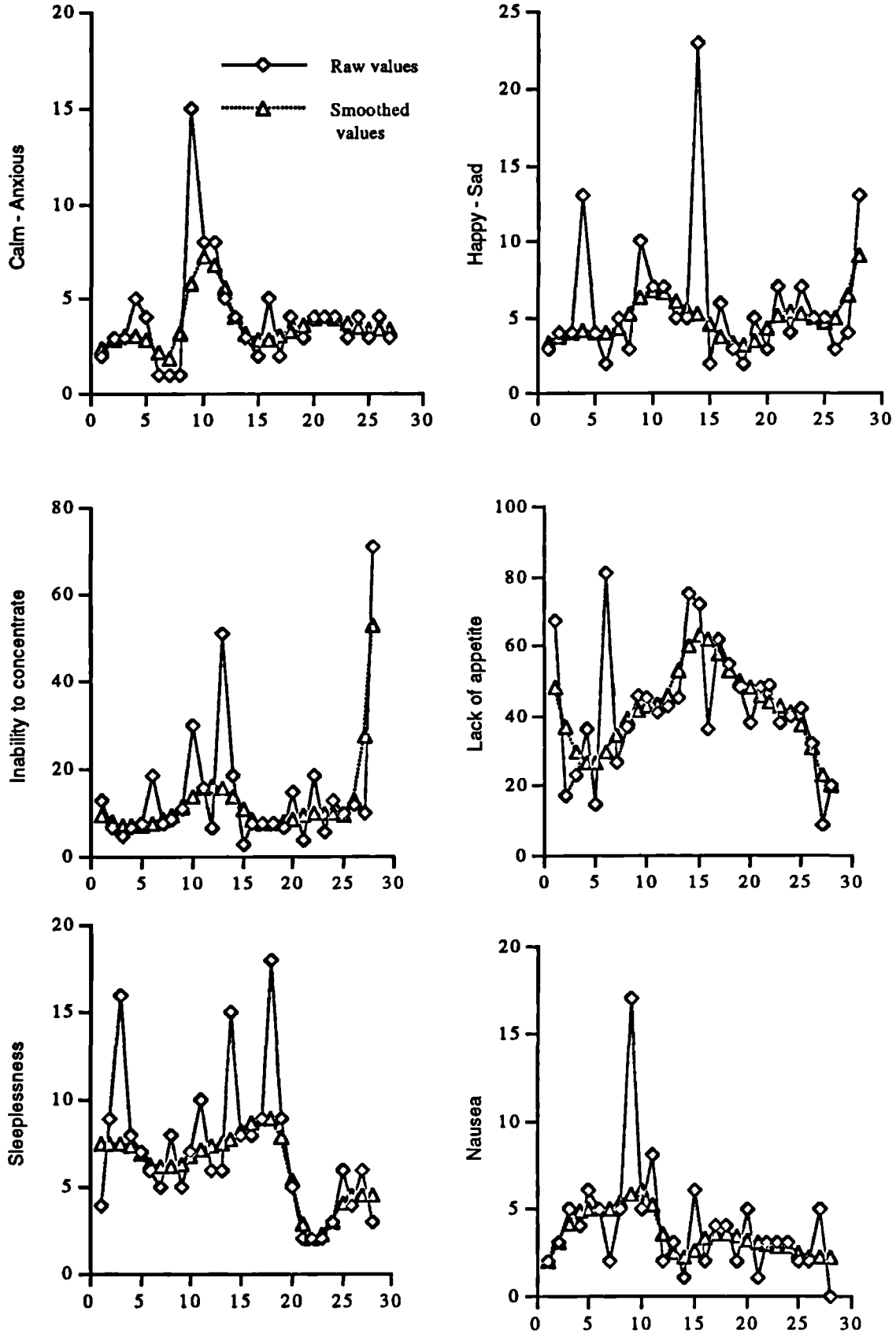
6.6.1.2 Subject 14

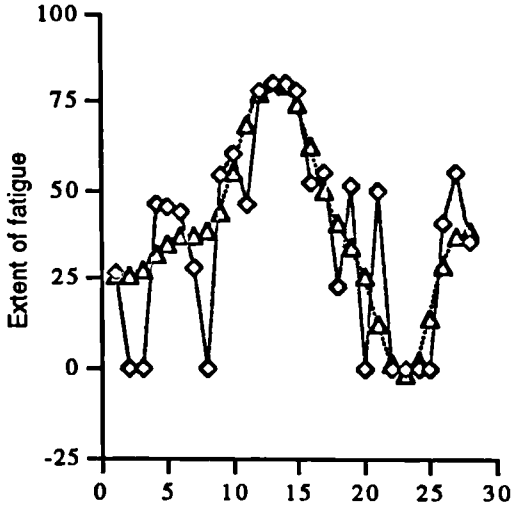
Subject 14 is a 61 year old man who has been receiving weekly injections of 5-Fu for colorectal cancer with multiple liver metastases for the last 5 months. The cancer was diagnosed over six months ago when he underwent laparotomy and right hemicolectomy. He lives with his wife and together they manage the daily chores although he admits that his wife assumes the main burden because he has sciatica. He plays an active role in the church and occasionally gives a sermon. He considers that tiredness and fatigue represented the same feelings. Fatigue had been a problem recently and he attributed this to his treatment and expected it to be a continuing problem. He felt his present fatigue was the same as the fatigue he had encountered prior to his illness and that there was nothing abnormal or unusual about it. It occurred every day but not for all of the day, tending to coincide with giving a sermon.

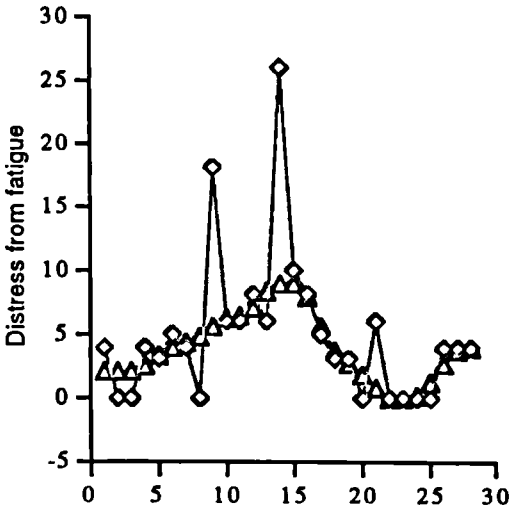
Fatigue fluctuated in a weekly cycle tending to rise in the days following an injection of chemotherapy on days 1, 7, 13, and 21 and fall to zero just before the next injection. *Diarrhoea* was reported as a constant problem throughout the diary-keeping period as was *pain* due to sciatica, both worsening during the 7–21 day period. During days 7–21 fatigue remained relatively high, attributed to an increase in *pain* and a very busy period in terms of work which necessitated travelling long distances. The additional VASs depict a relatively *calm* and *happy* person little troubled by *nausea* or *poor sleep*, although a *lack of appetite* seemed to persist ($\bar{x}$ = 42.4, SD = 17.9). This underlying profile of clear episodes of fatigue following the administration of chemotherapy is typical of many subjects receiving weekly injections of 5-Fu.

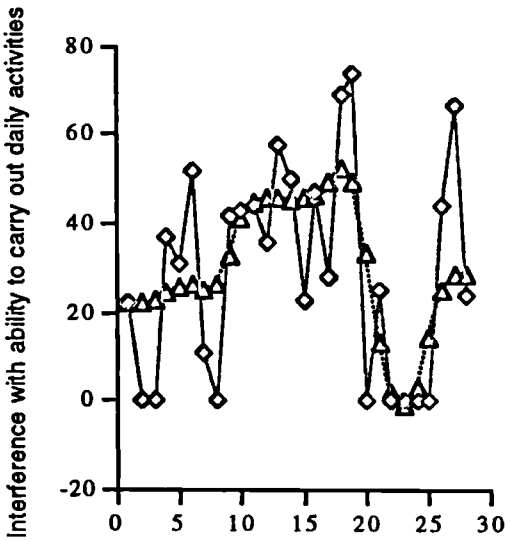
The subject felt his health status on the whole had remained stable during the data collection period and things at home were the same. He commented that his fatigue had not significantly altered and that it was caused by sciatica, a pre-existing health problem. When pressed on whether he had done anything that helped, he admitted that just sitting and resting in a chair with the occasional sleep during the day tended to dissipate his fatigue although he did not record this in his diary.

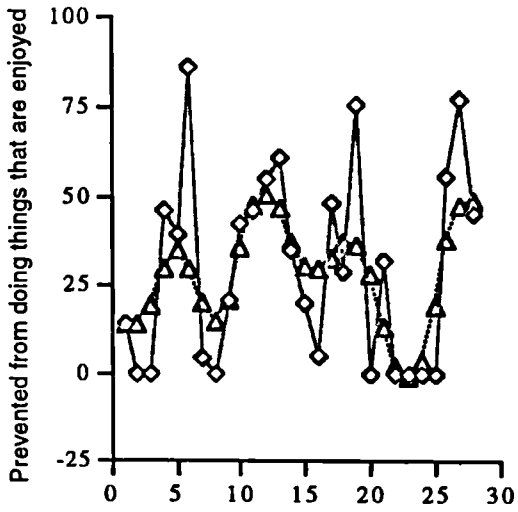
Figure 6.3 Pattern of daily diary items and summary statistics for subject 14

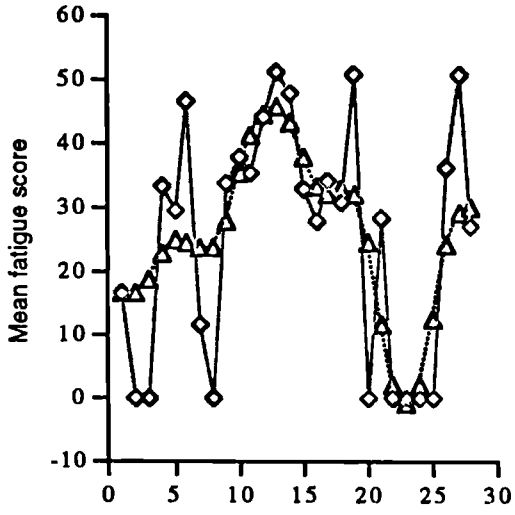












Summary statistics

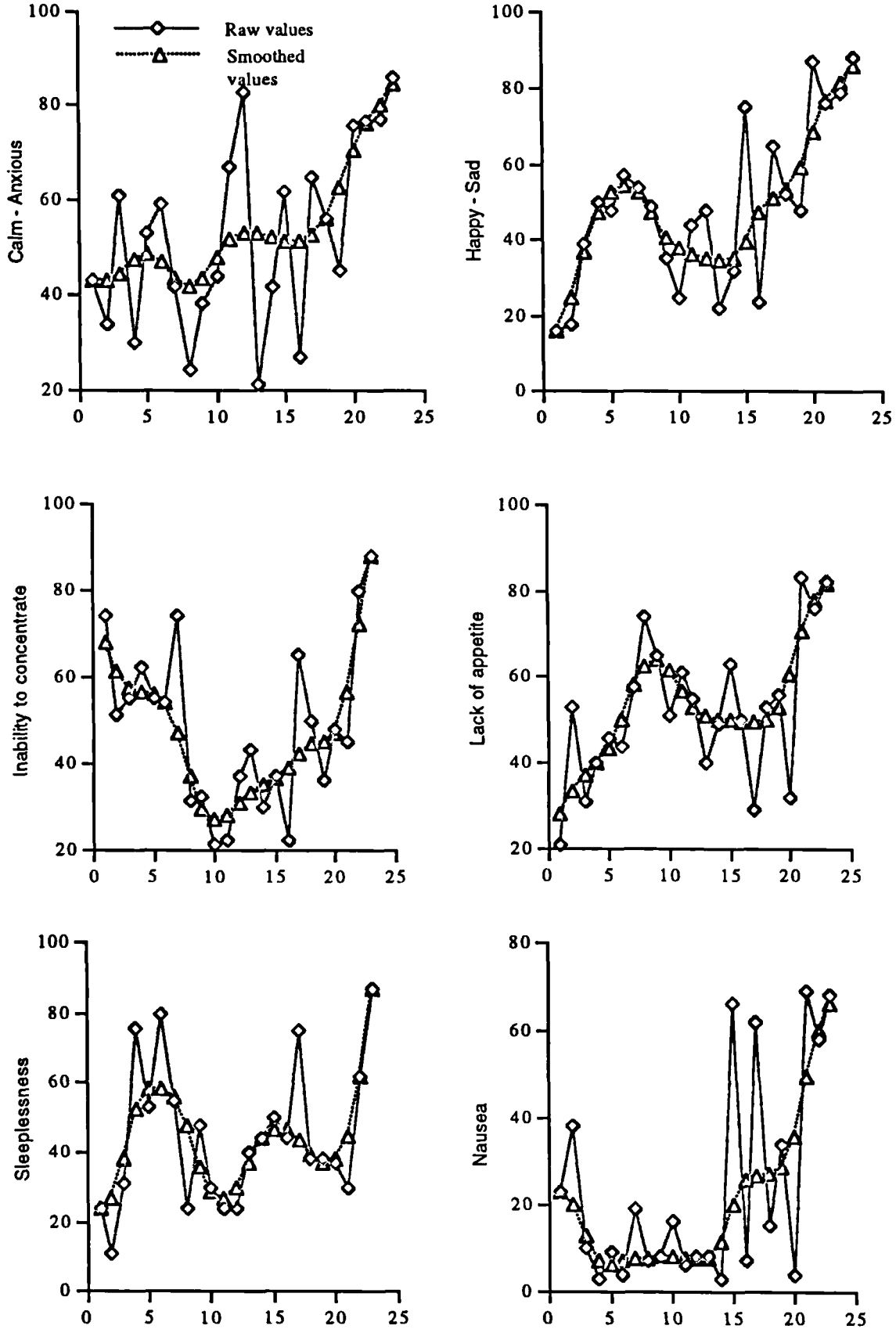
Variable	Mean	SD
Calm-anxious	4.2	2.9
Happy-sad	5.9	4.4
Concentration	14.4	14.6
Appetite	42.4	17.9
Sleeplessness	7.0	4.0
Nausea	3.9	3.1
Extent	36.8	27.7
Distress	4.9	5.7
Daily activities	29.5	23.8
Hobbies	29.9	27.2
Mean FS	25.3	18.7

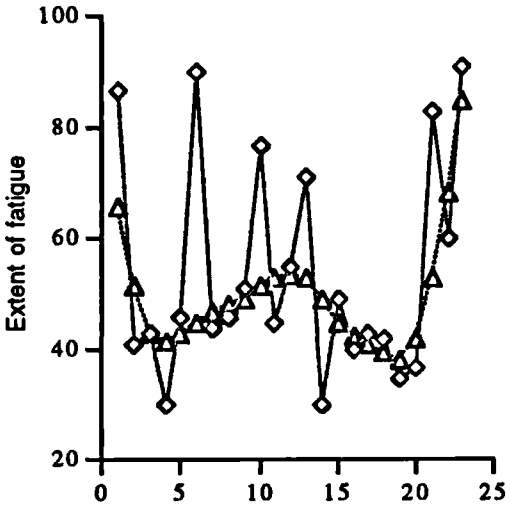
6.6.1.3 Subject 30

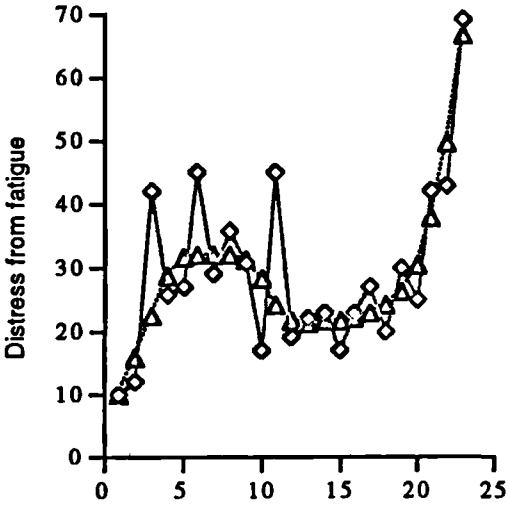
Subject 30 is a 58 year old lady with Stage IV ovarian cancer (liver and lung metastases). She is commencing her second pulse of palliative Carboplatin. She had been diagnosed just under a year ago and in that time had received 2 pulses of high dose Carboplatin and later 5 pulses of oral Etoposide. She lives with her husband and relied on him to do most of the household chores. Her daughters assisted with the shopping. She had given up work due to ill health. Fatigue was a constant problem every day, persisting for nearly all of the day except first thing in the morning. She felt that a mixture of things were linked with her fatigue ; the illness, treatment and in particular her lack of appetite. The anti-emetic tablets added to the fatigue, a comment often made by other subjects. In her opinion tiredness and fatigue were not synonymous: fatigue was a much more pronounced mental and physical feeling. The fatigue she experienced in association with her illness was perceived as being different (but not worse) and normal.

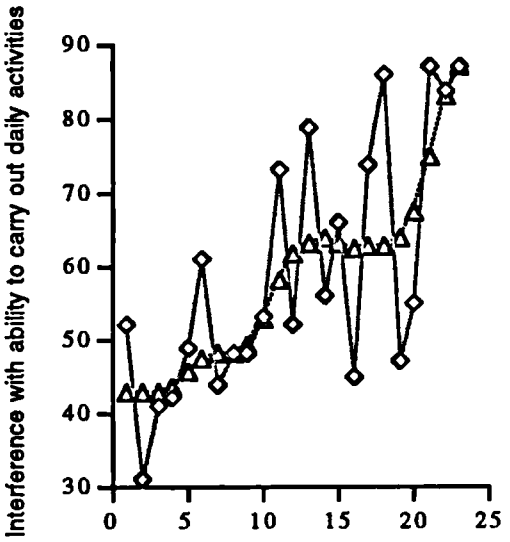
Sadly subject 30 died following this pulse of chemotherapy a few days after the last diary recordings, having been admitted to hospital on day 15. Her daughters returned the diary to the researcher by post adding a note that they wished the diary to be included in the study. They had helped their mother complete it for as long as possible. The VASs depict an escalating pattern in terms of *fatigue*, *mood* and other symptoms. During the last days she was particularly troubled by a cough, deep vein thrombosis and lack of appetite. She emphasised her lack of appetite and the chemotherapy as contributing to her fatigue.

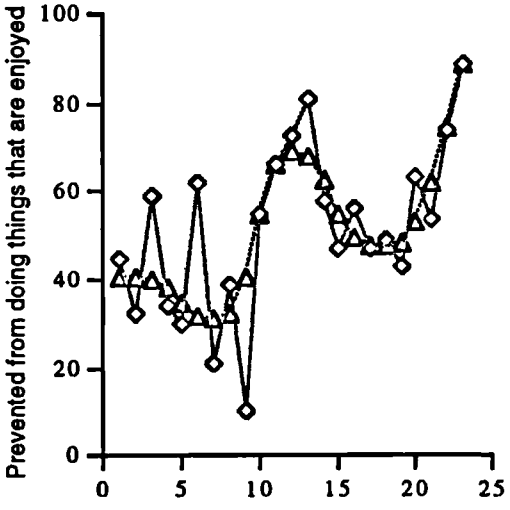
Figure 6.4 Pattern of daily diary items and summary statistics for subject 30

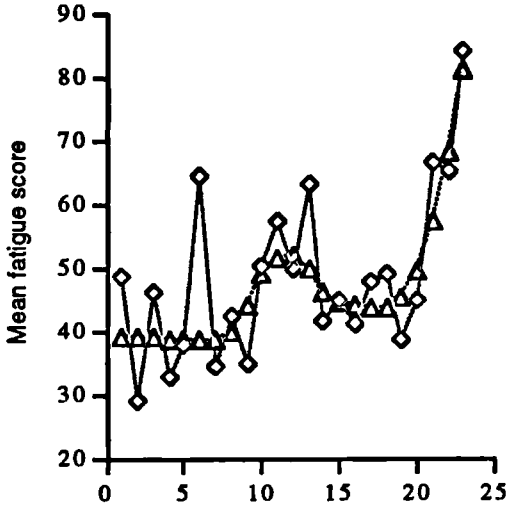












Summary statistics

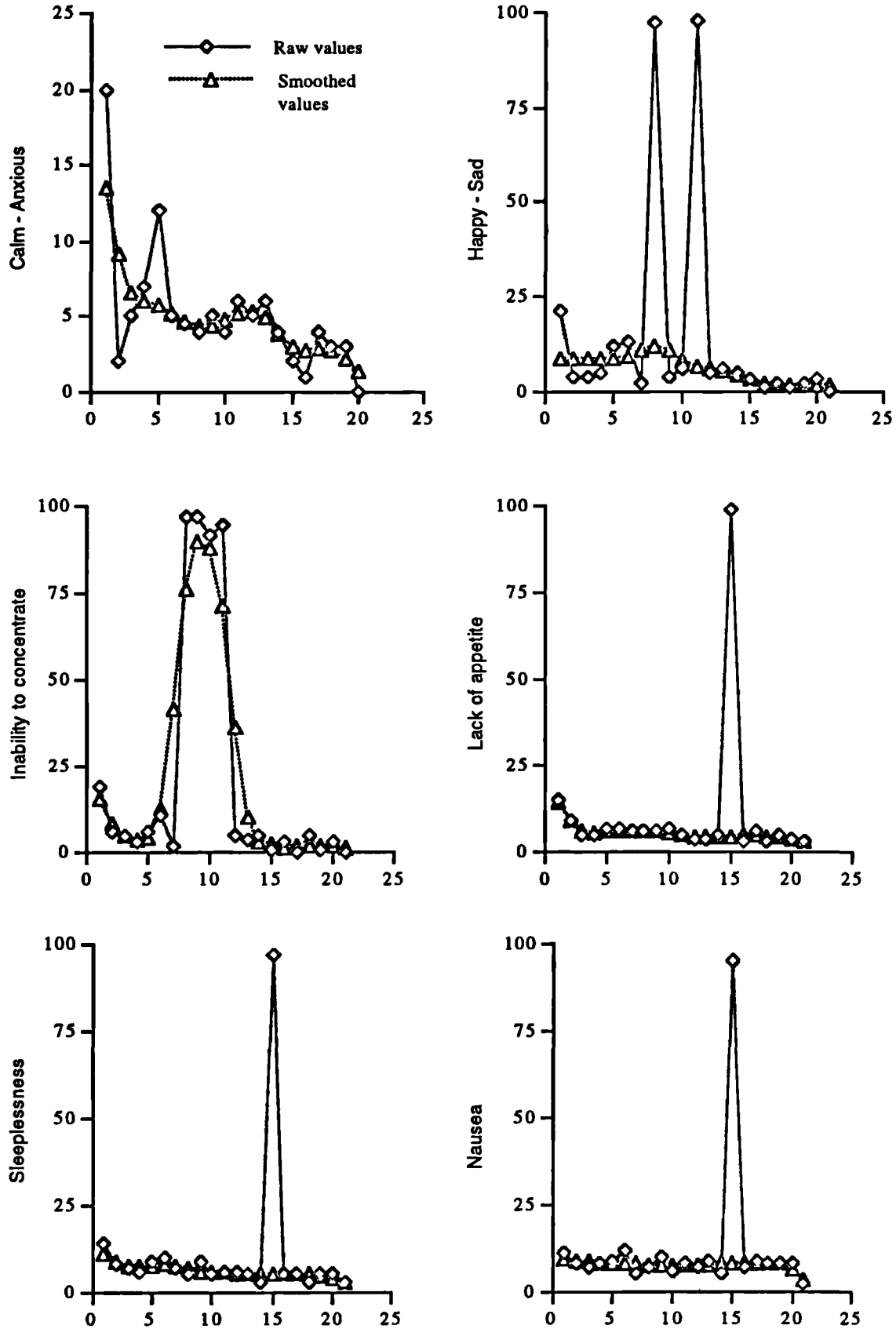
Variable	Mean	SD
Calm-anxious	5.6	19.9
Happy-sad	49.2	21.6
Concentration	48.4	19.0
Appetite	52.7	16.6
Sleeplessness	44.6	20.3
Nausea	23.7	23.9
Extent	53.8	19.5
Distress	29.6	13.4
Daily activities	59.1	16.9
Hobbies	51.6	19.0
Mean FS	48.5	13.1

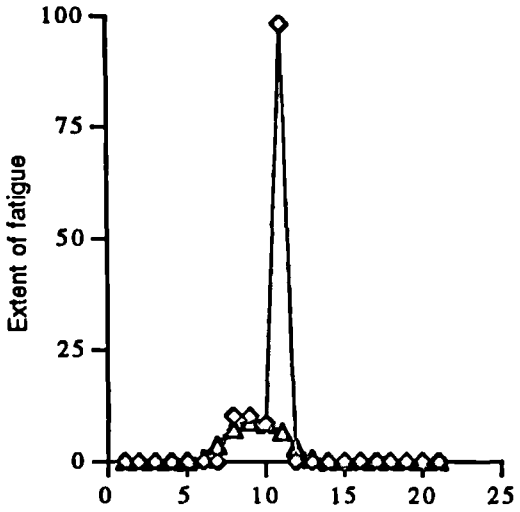
6.6.1.4 Subject 74

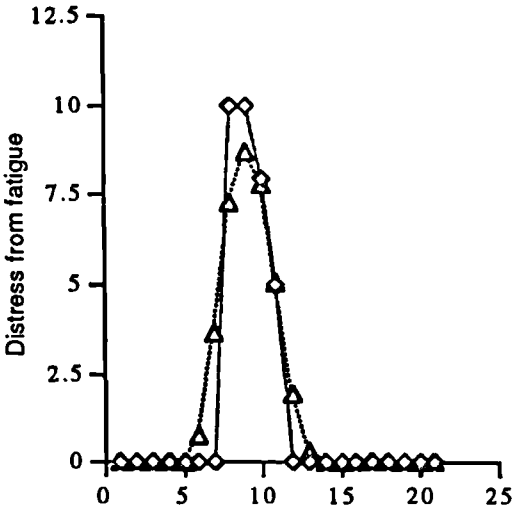
Subject 74 is male, 58 years old with a diagnosis of duodenal carcinoma. He was diagnosed just over six months ago when he underwent a laparotomy. He was prescribed a course of chemotherapy with the expectation that further surgery would follow. No distant metastases were evident and chemotherapy was considered non-palliative. He was scheduled to receive his fourth course of ECF. He lived at home with his wife, his $1\frac{1}{2}$ year old son and his housebound mother. He felt he was managing around the house as much as normal and did not consider his mother to make extra demands on his time and energy: in fact she was extremely supportive and they helped one another. The subject had retired from work on medical grounds. He felt tiredness and fatigue were the same phenomenon and admitted to experiencing fatigue for a few days after each pulse of chemotherapy particularly in the afternoon and early evening, particulalry whilst he continued to take the oral Etoposide. He perceived his present fatigue to be associated with the treatment and to be different than feelings of fatigue experienced prior to this illness, and because of this, considered it unusual.

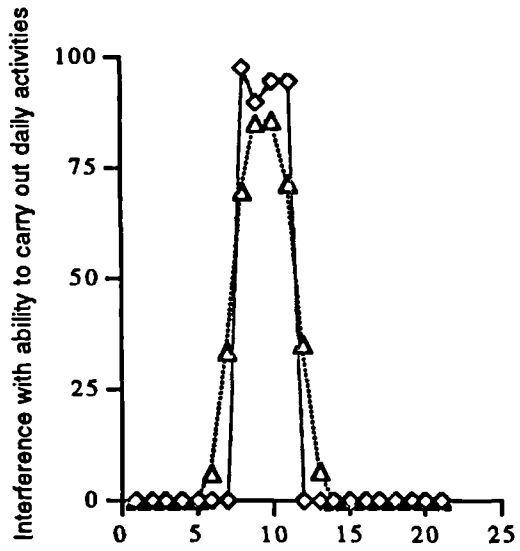
This subject presents a steady and positive evaluation of his *mood, symptoms* and *fatigue* during the diary period except for a severe episode of fatigue around days 8–11 and a corresponding *lack of concentration* and increased feelings of *sadness*. Anti-emetic tablets are listed as contributing/causing fatigue on these days . Gardening and watching the television are listed as being undertaken as actions to relieve fatigue. These activities offered partial relief. When questioned about the stability of his health, he mentioned the period of sickness which he thought might be related to diet. Apart from this episode he felt relatively well, as he had during all of his chemotherapy. He felt distraction, such as gardening, was helpful in the relief of fatigue.

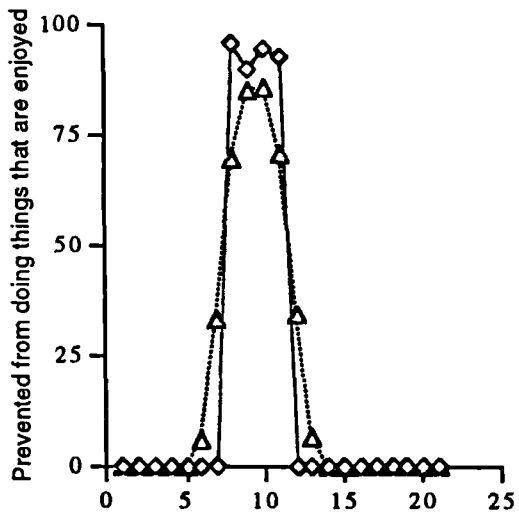
Figure 6.5 Pattern of daily diary items and summary statistics for subject 74

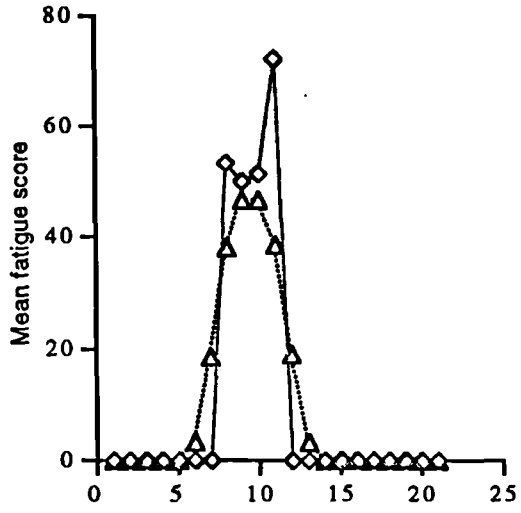












Summary statistics

Variable	Mean	SD
Calm-anxious	5.2	4.5
Happy-sad	14.0	8.2
Concentration	22.0	36.7
Appetite	10.2	20.5
Sleeplessness	10.6	20.0
Nausea	11.9	19.2
Extent	6.0	1.3
Distress	1.6	3.4
Daily activities	18.0	8.1
Hobbies	17.8	37.6
Mean FS	10.9	23.3

6.6.2 Patterns

All the individual plots were reviewed for basic features of change and *mean fatigue* plots based on the *type of chemotherapy* were generated from the aggregated data (see figure 6.6) where the number of subjects was greater than or equal to seven. The four individual fatigue VASs have not been reproduced here but are located in Appendix N (together with the remaining VASs from the diary), as the overall patterns were similar in each and the mean fatigue plot is considered to provide good representation of these data. A number of patterns have been identified.

6.6.2.1 Mirror/parallel shifts

Shifts in *extent of fatigue* are accompanied by corresponding shifts in the other VASs; as changes in the *extent of fatigue* occur they are closely mirrored by comparable changes in *distress from fatigue* and the level of *interference from fatigue with daily activities/chores* and other *enjoyable activities*. The *extent of fatigue* rating appears to be persistently higher than the ratings of these other dimensions. There also appear to be parallel shifts in one or more of the other VASs. There is seldom a lag, the shifts occur in tandem on the same day.

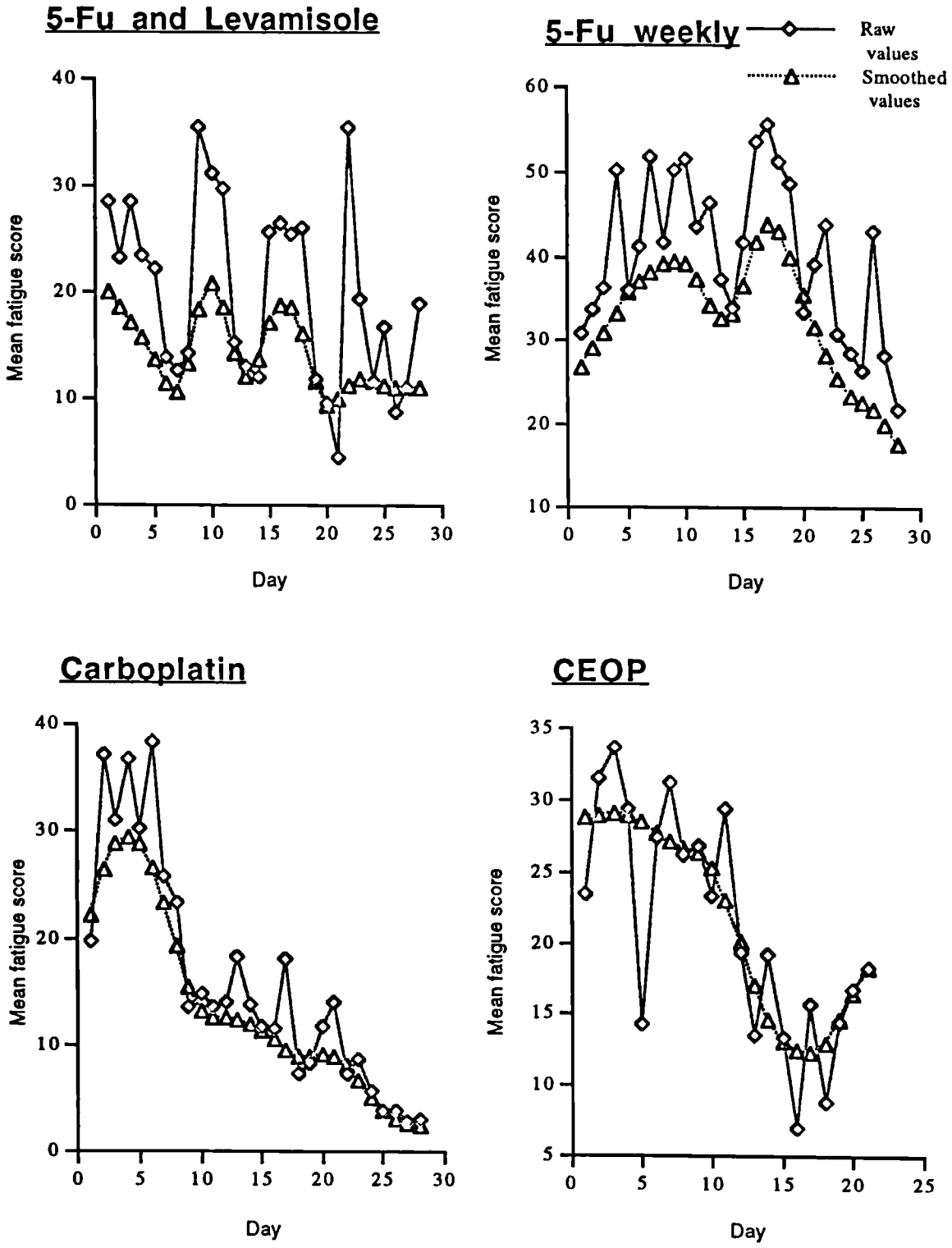
6.6.2.2 Large declines and improvements

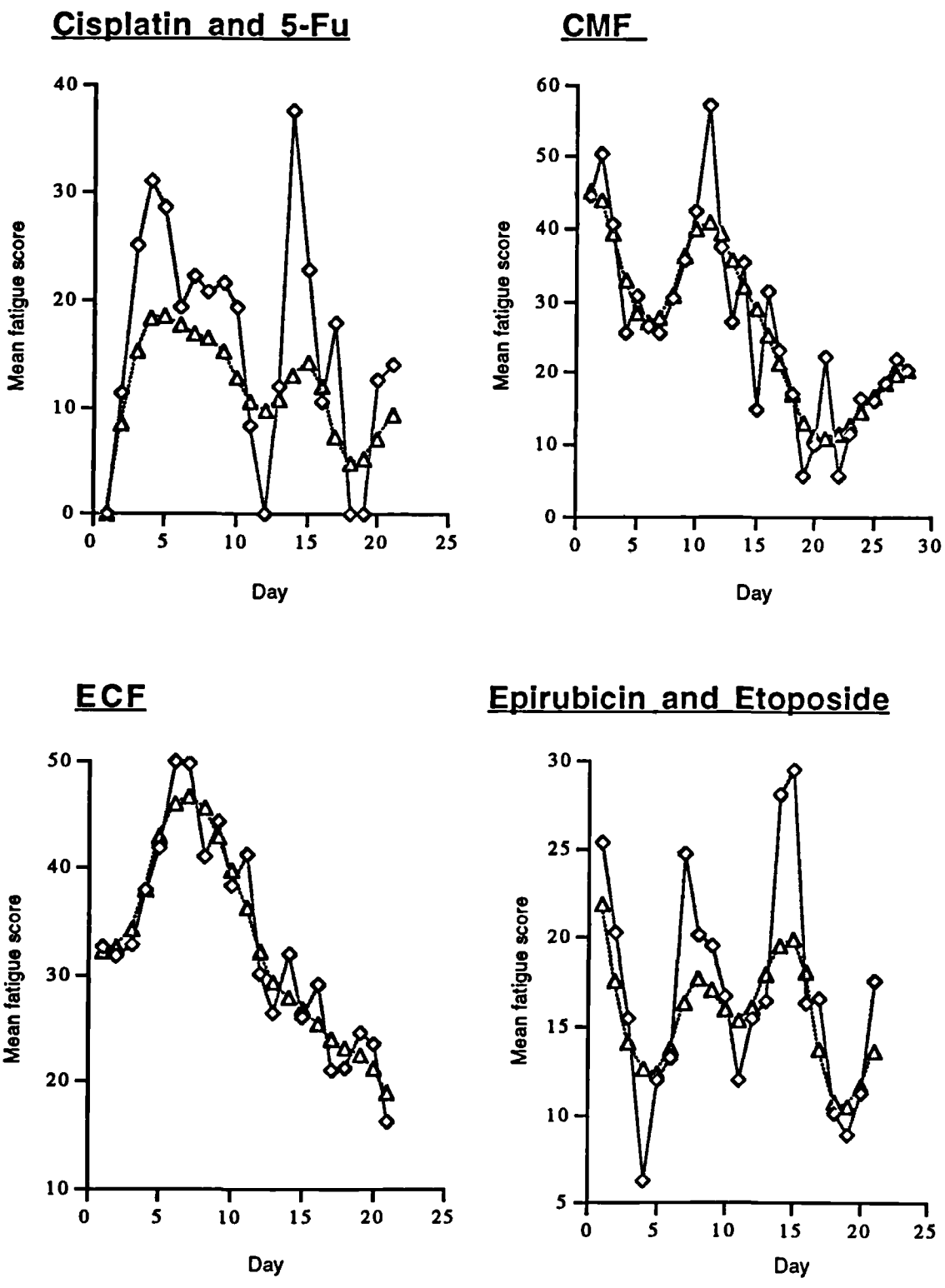
Increases in the *extent of fatigue* and the other dimensions tend to be large and abrupt and on the same day; they are rarely gradual. On the other hand, decreases are typically more gradual over several days.

6.6.2.3 Stability versus dynamism

People tend to have one basic mode for the diary period: either persistently stable, perhaps with a couple of days on which levels obviously fluctuate, or moderately/highly dynamic. Overall the plots show enormous variation in their degree of dynamics, the differential dynamics across people reflecting differences in the variables selected for measurement.

Figure 6.6 Pattern of *mean fatigue scores* by *type of chemotherapy* (raw and smooth plots)




Cisplatin and 5-Fu
Mean fatigue score
Day
CMF
Mean fatigue score
Day
ECF
Mean fatigue score
Day
Epirubicin and Etoposide
Mean fatigue score
Day

6.6.2.4 Dynamics at start, middle and end of diary

The administration of a bolus dose of chemotherapy often produces the most extreme *mean fatigue* value that an individual records during the diary period. For some, this occurs immediately following chemotherapy, and subsides after a few days . For others, the extreme *mean fatigue* value occurs a couple of days following administration. In those people receiving traditional bolus and/or short term infusion (CMF, Epirubicin and Etoposide, Carboplatin, CEOP, Cisplatin and 5-Fu) or bolus and continuous infusion (ECF), there is another abrupt increase in the *mean fatigue score* around the expected nadir period, and again just prior to the next pulse of chemotherapy as the diary period draws to a close. In people receiving weekly bolus injections of 5-Fu, a weekly cyclical pattern is evident with increases in fatigue coinciding with the administration of chemotherapy. The degree of *nausea* recorded exhibits a different pattern. It is common for extreme scores to be achieved during the first few days and *nausea* then gradually declines over the rest of the week.

When the aggregated plots in figure 6.6 are scrutinised it becomes apparent that distinct patterns emerge dependent on the *type of chemotherapy* the subjects receive - between group differences. Subjects receiving weekly chemotherapy (5-Fu weekly and 5-Fu and Levamisole) present a distinct and cyclical weekly pattern of fatigue, and interestingly those who have metastatic disease (the weekly 5-Fu protocol) appear to attain higher *mean fatigue scores* compared to those receiving adjuvant therapy (the 5-Fu and Levamisole protocol). Subjects receiving bolus and continuous chemotherapy experience fatigue which returns to a plateau $\bar{x} \approx 20$–30, which exceeds the fatigue experience of those receiving conventional pulsed chemotherapy. The latter appear to reach a fatigue level of an approximate $\bar{x} \approx$ 30–45 and this then declines returning to a plateau of between 0–20.

Subjects with breast cancer having CMF receive chemotherapy on day 1 and day 8 and take an oral drug on days 1–14. The pattern of fatigue reflects this in that fatigue remains relatively high for the first 14 days with a superimposed increase shortly after day 8. Subjects with a diagnosis of small cell lung cancer receiving the combination of Epirubicin and Etoposide appear not to be influenced by continuing to take oral Etoposide on days 1–4: fatigue subsides after day 1, rising again over days 5–7 and again during the expected nadir. The *mean fatigue score* rises sharply a few days before the next course of chemotherapy. This phenomenon also appears in those subjects receiving CMF, CEOP and Cisplatin and 5-Fu. The ovarian cancer subjects receiving single agent Carboplatin appear to experience fatigue during the first week post infusion, but

following this fatigue gradually declines, and particularly during the fourth week reaches a low level probably indicating that most of this sample do not experience fatigue during the latter stage of the cycle. The Cisplatin and 5-Fu regime for subjects with an unknown primary malignancy entails a 5 day continuous infusion of 5-Fu with Cisplatin administered over 4 hours on day 2. The *mean fatigue scores* remain raised during these five days with a gradual decline, followed later around days 13–15 and days 20–21 by increases in fatigue. Non-Hodgkin's lymphoma subjects receive bolus doses of chemotherapy on day 1 followed by a 5-day course of oral Prednisolone. On the cessation of the Prednisolone there appears to be a rise in the level of fatigue.

6.6.3 Time series analysis

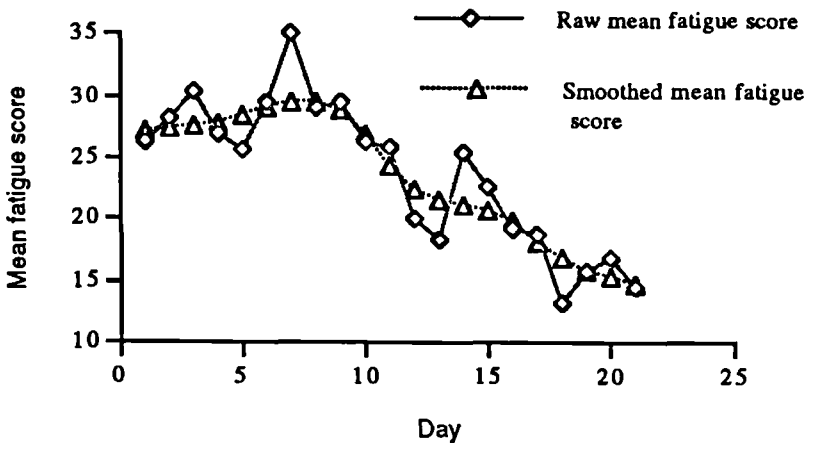
A time series is a collection of observations made sequentially in time. The flow charts provided by Abraham and Neundorfer (1990) were utilised in addition to the protocols offered by Dunstan (1993) to direct the analysis of time series. As suggested by Chatfield (1989) an appropriate expert was consulted, the time plots were examined to assess the more important features, and models were considered to see if they were consistent with empirical and theoretical knowledge and with the objectives of the investigation.

6.6.3.1 Plotting and transformation of data

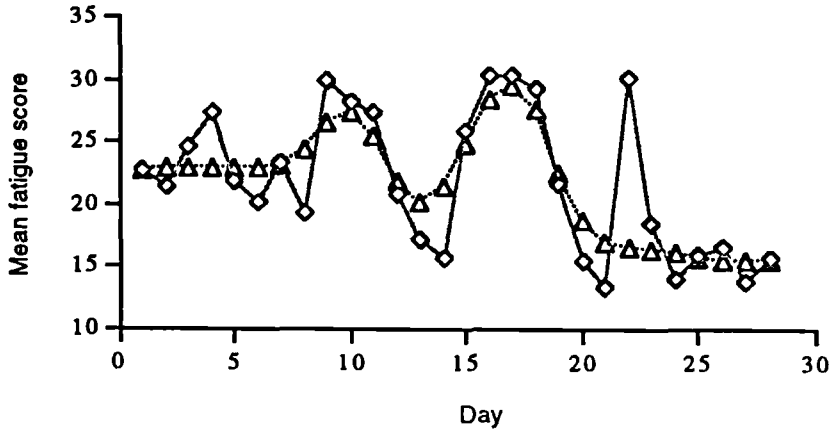
The first and most important step is usually to plot the data, to obtain simple descriptive measures of the main properties of the series and to gain an initial impression of the nature of the data. No data transformations were carried out as this would have been inappropriate due to the ordinal nature of these data. For the present series, 21, 28 and weekly cycles, the variation was dominated by obvious features (see figure 6.7 for plots of *mean fatigue scores* and Appendices O, P and Q for the remaining daily variables). The weekly series ($n=17$) exhibits a cyclical pattern that is repeated typically every 7 days. During the 7-day period the variation was choppy rather than smooth, and the effect of smoothing can be seen most clearly during the second and third cycle. The 21-day ($n=61$) and 28-day ($n=31$) series exhibit a persistent tendency to decrease over time but there are some changes in the behaviour of the series. The rate of decline in the *mean fatigue score* appears to slow around day 10–15 and again after day 19 in the 28-day series. In the 21-day series the decline in the *mean fatigue score* does not begin to occur until after day 10.

Figure 6.7 Time plots of raw and "smoothed" *mean fatigue scores* of subjects receiving a 21-day, 28-day and weekly cycle of chemotherapy

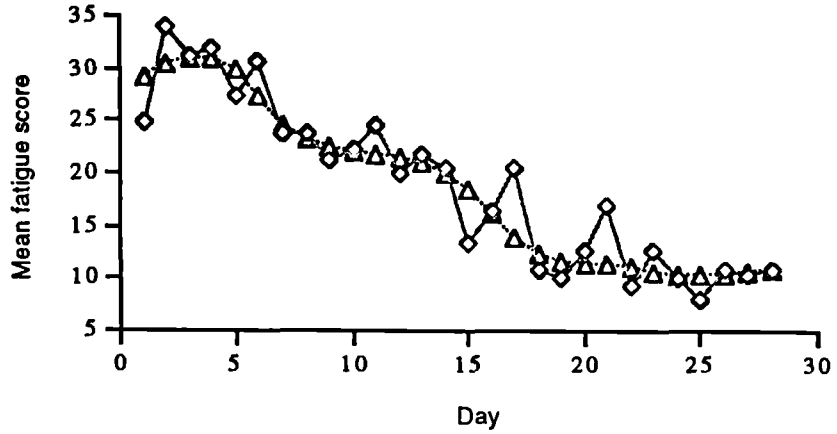
a) 21-day (*n* = 61)



b) Weekly (*n* = 17)



c) 28-day (*n* = 31)



6.6.3.2 Secular trend and seasonality

The plots were examined for secular trend, seasonal and other cyclical variations. There are three major approaches to the removal of a secular trend and seasonality from a time series: curve fitting, linear filtering and differencing. Linear filtering, where a time series with trend is converted into a "smooth" time series devoid of trend related fluctuation, was used and the effect of smoothing can be visualised in figure 6.7. The trend for a decreasing *mean fatigue score* following chemotherapy administration and the weekly cyclical variation in the weekly chemotherapy group were considered an important aspect of the phenomenon being studied and thus were analysed as an integral part of the change process and the time series. Thus curve fitting was not pursued. A special type of filtering, called differencing was examined. Differencing is acknowledged as being particularly useful for removing a trend. A given time series is differenced until it becomes stationary. This is a widely used method and an integral part of the procedures advocated by Box and Jenkins (1976). For non-seasonal data, first-order differencing is usually sufficient to attain apparent stationarity, so that the new series is formed from the original series $\{X_1,\ldots,X_n\}$ by $Y_t = X_{t+1} - X_t = \nabla X_{t+1}$ i.e. the previous observation is subtracted from the current one. If there is a linear trend, then this should be removed by such a difference. Differencing was found not to produce any simplification of the series.

6.6.3.3 Identifying the ARIMA model

The AutoRegressive Integrated Moving Average(ARIMA) class of models incorporate three components : the possibility of differencing(I) and estimation of a day's observation in terms of previous observations(AR) and in terms of disturbances from predicted values in the past(MA). The most general ARIMA model involves all three processes. Each is described by a small integer. The general model, neglecting seasonality is traditionally written ARIMA(p,d,q), where p is the order of autoregression, where $d$is the degree of differencing, and q is the order of moving average involved. In the $d$differenced series , $p$previous observations and $q$previous disturbances are used to predict the current value. Although such models appear rather daunting, in most practical cases the values of p and q are small and fitting such as model is relatively easy with the computer package of Minitab. If q= 0 the model is said to be an autoregressive process of the order p (abbreviated to AR(p)), while if p= 0 it is a moving average model of order q(MA(q)). The procedure for fitting an autoregressive model is very like that for a regression model, but when there is a moving average component there are considerable theoretical and practical difficulties (Dunstan, 1993).

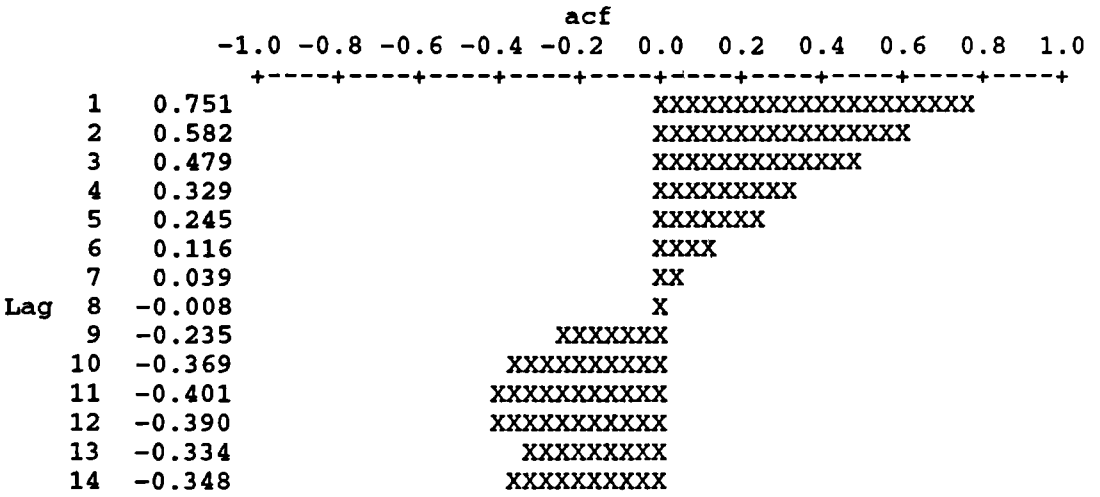
The real problem is knowing which model to fit in the first place. It has already been concluded above that differencing would not be helpful, thus parameter d is set to zero. Hence, the AR(p) and MA(q) parameters must now be considered. In determining suitable values for these the autocorrelation coefficient and partial autocorrelation coefficient are useful.

6.6.3.4 Autocorrelation

An important guide to the properties of a time series is provided by a series of quantities called sample autocorrelation coefficients (acf), which measure the correlation between observations at different distances apart. Autocorrelation determines the degree of association between X_t and X_{t+k} , where k represents different time lags, 0, 1, 2 ... up to $k << n$. A large autocorrelation r_k implies high association for the observations at k time points apart.

A useful aid to interpreting a set of autocorrelation coefficients is a graph called a correlogram in which r_k is plotted against the lag k. Interpretation of the autocorrelation function was undertaken with the assistance of an experienced statistician . As with ordinary correlation coefficients, values must lie between −1 and +1, with values near these extremes indicating a high degree of linear dependency. Values closer to zero suggest values that are more or less independent. Figure 6.8 illustrates the autocorrelation coefficients for the *mean fatigue score* in relation to the 21-day cycle. A similar pattern was evident for the 28-day cycle.

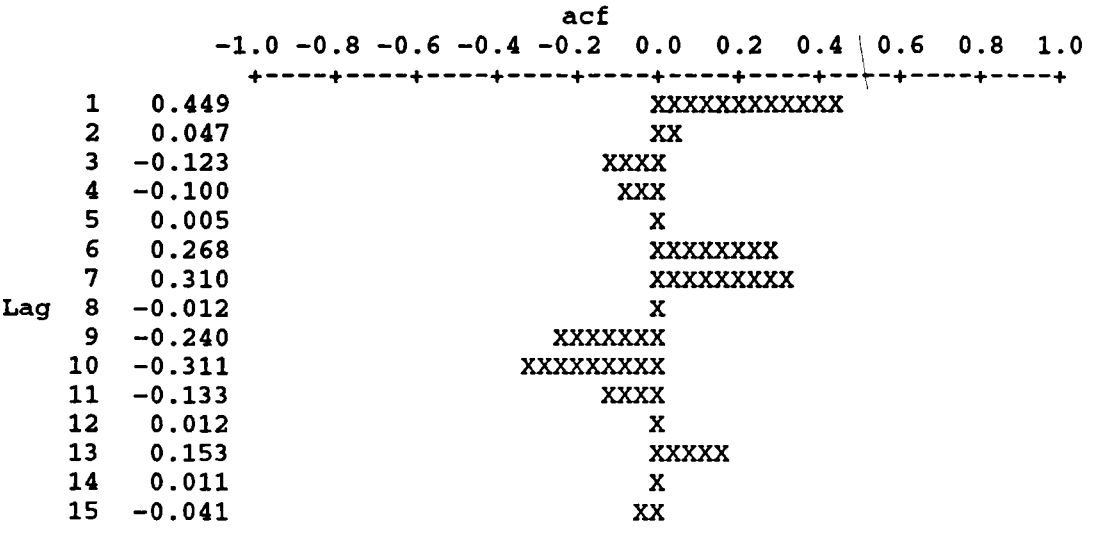
Figure 6.8 Autocorrelation coefficient of *mean fatigue score* for the 21-day cycle



It appears that the observations made on a given day bear the strongest relation to observations made the next day (k=1). The autocorrelation subsides gradually and stays low.

Inspection of the autocorrelation function of the *mean fatigue score* for the weekly cycle revealed an additional influence to that outlined above. A seasonal element was evident, recognisable by the regular peaks in the autocorrelation function, coinciding with the weekly administration of chemotherapy (see figure 6.9). This suggests that not only is there a residual effect from the way a subject felt yesterday, but in addition events at the same stage in the last chemotherapy cycle exert a direct influence on the *mean fatigue score*.

Figure 6.9 Autocorrelation coefficient of *mean fatigue score* for the weekly cycle



However, this explanation does not hold for the remaining variables in subjects receiving weekly chemotherapy, namely aspects of *mood*, *appetite*, *sleep* and *concentration*. Inspection of the relevant autocorrelation function suggested that in the case of the variable *concentration*, the autoregressive element was not present. Only a seasonal element was evident in this case (see figure 6.10). It was not possible to offer any meaningful interpretation of the remaining autocorrelation functions in relation to the weekly cycle of chemotherapy.

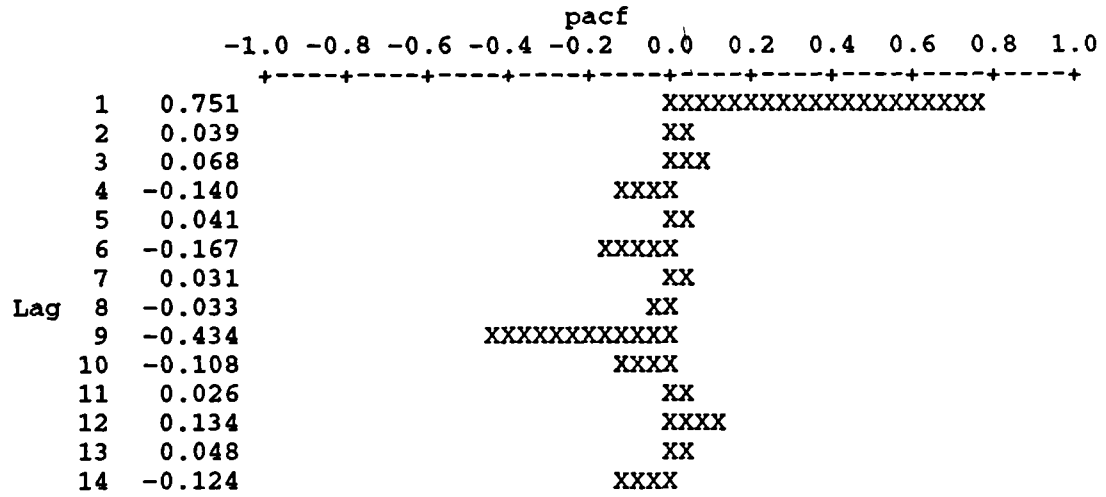
Figure 6.10 Autocorrelation coefficient of *concentration* for the weekly cycle

```
                                    acf
          -1.0 -0.8 -0.6 -0.4 -0.2  0.0  0.2  0.4  0.6  0.8  1.0
            +----+----+----+----+----+----+----+----+----+----+
     1   0.114                          XXXX
     2   0.148                          XXXXX
     3  -0.206                       XXXXXX
     4  -0.162                        XXXXX
     5   0.090                           XXX
     6   0.237                           XXXXXXX
     7   0.447                           XXXXXXXXXXXX
Lag  8  -0.145                        XXXXX
     9  -0.038                          XX
    10  -0.292                      XXXXXXXX
    11  -0.042                          XX
    12   0.018                           X
    13   0.129                          XXXX
    14   0.033                          XX
    15  -0.214                       XXXXXX
```

6.6.3.5 Partial autocorrelation coefficient

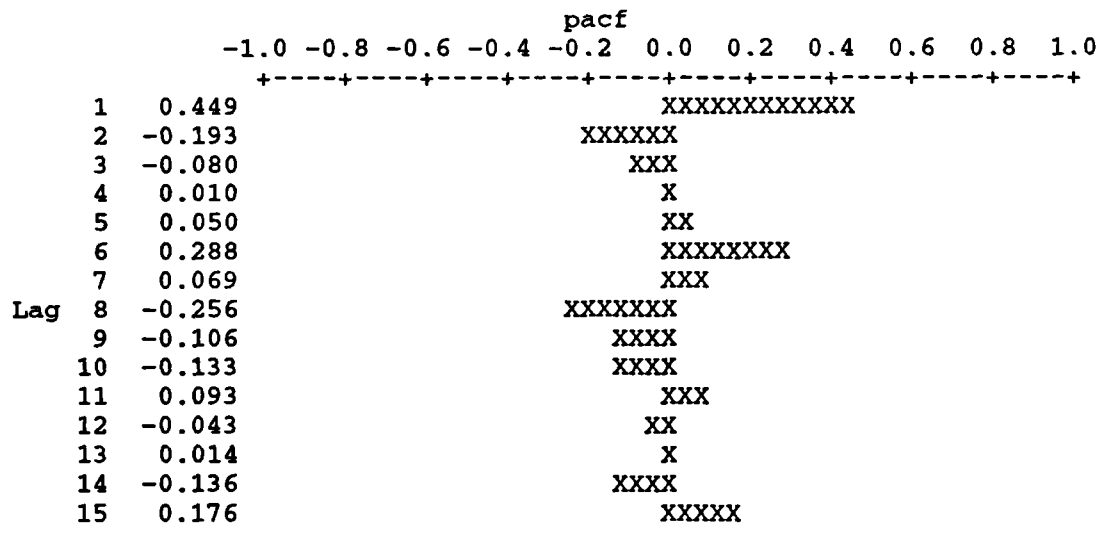
It is difficult to assess the order of an AR process from the sample autocorrelation function alone. The partial autocorrelation function (pacf) can be used as an aid to determining the order of the AR process and measures the degree of association between X_t and X_{t+k} allowing for the relationships with the time points between. The correlation between X_t and X_{t+2} is partly due to the dependence of both on X_{t+1}. The partial correlation coefficient attempts to isolate the direct relationship between X_t and X_{t+k}. The partial autocorrelation function for the *mean fatigue score* for the 21-day time series is displayed in figure 6.11.

Figure 6.11 Partial autocorrelation function of *mean fatigue score* - 21-day cycle



In figure 6.11 the partial autocorrelation function is rather small after the first value. The autocorrelation and partial autocorrelation functions are typical of an AR(1) model, that is a first-order regressive process where only the single preceding value is used. Thus this model has an AR parameter of 1, and MA parameter of 0.

Figure 6.12 Partial autocorrelation function of *mean fatigue score* - weekly cycle



It is evident in figures 6.11–6.13 that in each case the partial autocorrelation is low for all lags. This is typical of models with no MA component. This was confirmed later when the ARIMA models were fitted and the MA parameter was not significantly different from zero.

Figure 6.13 Partial autocorrelation function of *concentration* - weekly cycle

```
                                  pacf
          -1.0 -0.8 -0.6 -0.4 -0.2  0.0  0.2  0.4  0.6  0.8  1.0
            +----+----+----+----+----+----+----+----+----+----+
     1   0.114                          XXXX
     2   0.137                          XXXX
     3  -0.244                    XXXXXXX
     4  -0.144                      XXXXX
     5   0.216                          XXXXXX
     6   0.246                          XXXXXXX
     7   0.340                          XXXXXXXXXX
Lag  8  -0.364                   XXXXXXXXXX
     9  -0.083                       XXX
    10   0.028                         XX
    11   0.067                         XXX
    12  -0.192                     XXXXXX
    13  -0.140                      XXXX
    14  -0.038                        XX
    15   0.043                         XX
```

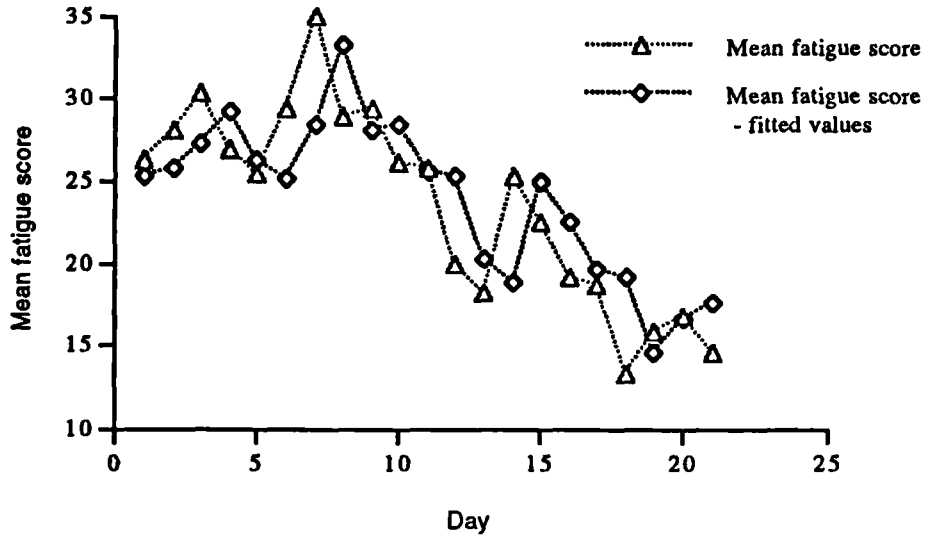
6.6.3.6 Model estimation

Thus in relation to the 21 and 28-day cycle an ARIMA(1,0,0) model is generated. The ARIMA command in Minitab which fits models to a time series confirmed that the AR(1) model gave the best representation of the observed time series (see figure 6.14) for the 21-day and 28-day series. This is a relatively uncomplicated model, which attempts to describe a trend. This is perfectly adequate to describe the variation in the time series, and clarifies the main properties of the series. That is, the autocorrelations, r_1, r_2, r_3,... appear to be decreasing exponentially. An examination of the combined plots of the raw data and fitted values in figure 6.15 provides a visual representation of the degree of fit.

Figure 6.14 Minitab output confirming an AR(1) model for *mean fatigue score* (21-day cycle)

```
MTB> ARIMA 1 0 0 'Mean fatigue score'

Final Estimates of Parameters[ab]
Type        Estimate    St. Dev.   t-ratio
AR   1        0.86        0.14       5.97
Constant      3.14         .82       3.82
Mean         22.50        5.89

Modified Box-Pierce chisquare statistic[c]
Lag                  12
Chisquare     5.9(df=11)

[a] The model is fitted by an iterative process, that is estimates of parameters
 are progressively improved by comparing fitted and observed values

[b] The autoregressive coefficient equals .86. The t-ratio (the ratio of each
 estimate to its standard deviation) in this case is large, therefore neither
parameter is zero. This is significant.

c A test statistic that tests the null hypothesis that a set of autocorrlations
are associated with a random series. In the above it is non-significant for the
residuals and therefore there is no lack of fit
```

Figure 6.15 Time series plots of raw data and fitted values for *mean fatigue score* (21-day cycle)



However, as suggested by the autocorrelation function for the *mean fatigue score* of the weekly data set an AR(1) model does not entirely explain the behaviour of these series, the resulting parameter estimates being unsatisfactory. A change in specification

is necessary. A seasonal element was introduced and thus the model specification was ARIMA(100,100,7) (see figure 6.16). The value of 7 denotes the weekly chemotherapy cycle.

Figure 6.16 Minitab output confirming an AR(1) model with a 7-day seasonal element for *mean fatigue score* (weekly cycle)

MTB> ARIMA 1 0 0 1 0 0 7 'Mean fatigue score'

Final Estimates of Parameters[ab]

Type		Estimate	St. Dev.	t-ratio
AR	1	0.45	0.19	2.42
SAR	1	0.54	0.25	2.20
Constant		5.35	0.94	5.70
Mean		21.35	3.74	

Modified Box-Pierce chisquare statistic[c]

Lag	12
Chisquare	4.3 (df=10)

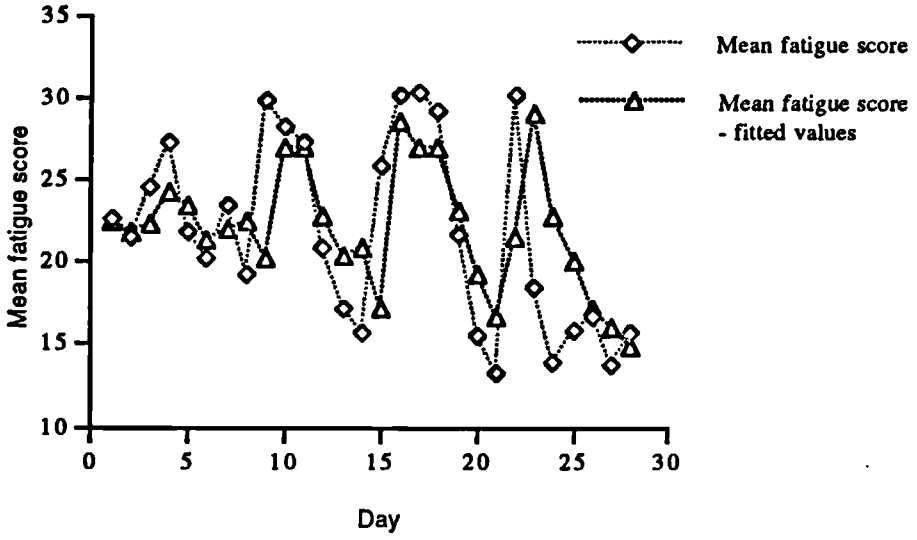
[a] The model is fitted by an iterative process, that is estimates of parameters are progressively improved by comparing fitted and observed values

[b] The autoregressive coefficient equals .45 and the seasonal autoregressive coefficient equals .54. The t-ratio in this case is moderate, therefore neither parameter is zero. This is significant.

c A test statistic that tests the null hypothesis that a set of autocorrelations are associated with a random series. In the above it is non-significant for the residuals and therefore there is no lack of fit

An examination of the combined plots of the raw data and fitted values in figure 6.17 provides a visual representation of the degree of fit.

Figure 6.17 Time series plots of raw data and fitted values for *mean fatigue score* (weekly cycle)



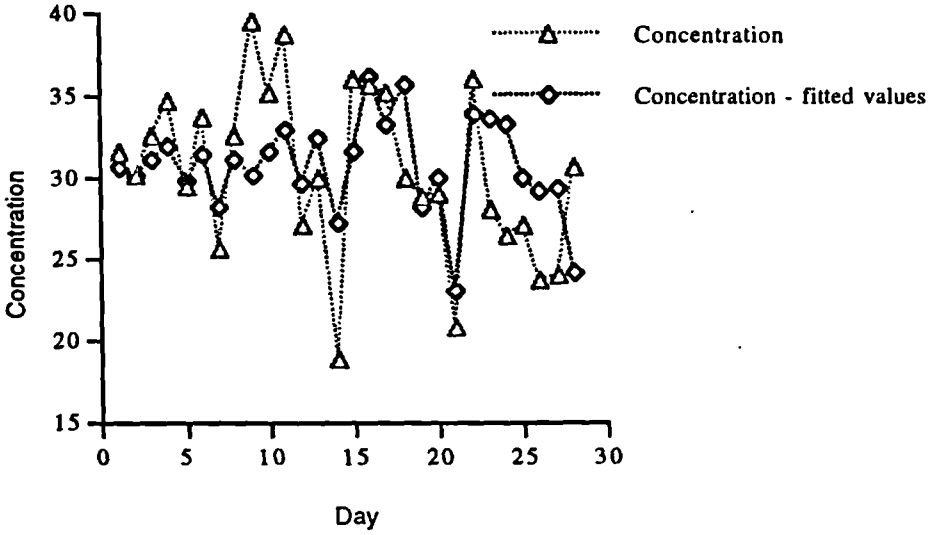
Ultimately it was only rational to suggest one further model in the weekly data series. This related to the variable concentration. The model specification for concentration was ARIMA(000,100,7) and confirmation is evident in figure 6.18. In this case only the seasonal element was prominent.

Figure 6.18 Minitab output confirming a 7-day seasonal model for *concentration* (weekly cycle)

```
MTB> ARIMA 0 0 0 1 0 0 7 'Concentration'

Final Estimates of Parameters[ab]
Type        Estimate    St. Dev.   t-ratio
SAR  1        0.64        0.18       3.48
Constant     10.93        2.31      12.97
Mean         21.35        3.74

Modified Box-Pierce chisquare statistic[c]
Lag                  12
Chisquare     6.0 (df=11)

[a] The model is fitted by an iterative process, that is estimates of parameters
 are progressively improved by comparing fitted and observed values

[b] The seasonal autoregressive coefficient equals .64.  The t-ratio in this case
 is moderate, therefore neither parameter is zero.  This is significant.

c A test statistic that tests the null hypothesis that a set of autocorrelations
are associated with a random series.  In the above it is non-significant for the
residuals and therefore there is no lack of fit
```

A visual representation of the degree of fit is presented in figure 6.19, which depicts plots of the fitted and raw data values for the weekly *concentration* time series

Figure 6.19 Time series plots of raw data and fitted values for *concentration* (weekly cycle)

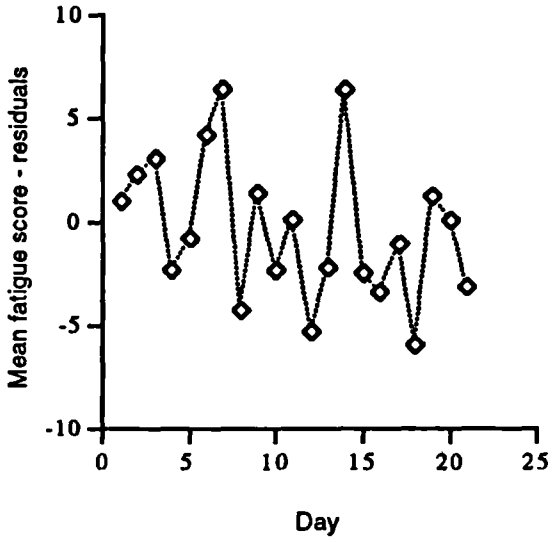


6.6.3.7 Model checking

Once a particular model has been identified, the next step is to determine if the selected model provides an adequate description of the data. This is done by the examination of residuals. Residuals are differences between the actual observations and the model fitted values. Significance tests have been developed which use the autocorrelation of the residual values to determine the goodness of fit. The Minitab procedure automatically calculates the residuals and the Modified Box-Pierce chi-square statistic is applied to these values. The test statistic is based on a number, say k, of the squared autocorrelations of the residuals. The statistic produced has, under the hypothesis of the model fitted being correct, an approximate chi-squared distribution, with degrees of freedom equal to $k-p-q$. The parameter estimates in the case of the 21-day and 28-day cycle series were satisfactory in nearly all cases on statistical grounds (see figure 6.14 for an example of this). Occasionally there were computational problems with the data. Having carried out the above tests, it is advisable to make a visual inspection of the residuals and their correlogram. These are shown in figure 6.20 a and b. There is no obvious pattern in the residuals and the autocorrelations are all low, apparently confirming the appropriateness of the model selected.

Figure 6.20 a) Residuals from fitting an AR(1) model to the 21-day *mean fatigue score* series and b) the correlogram of the residuals

a)



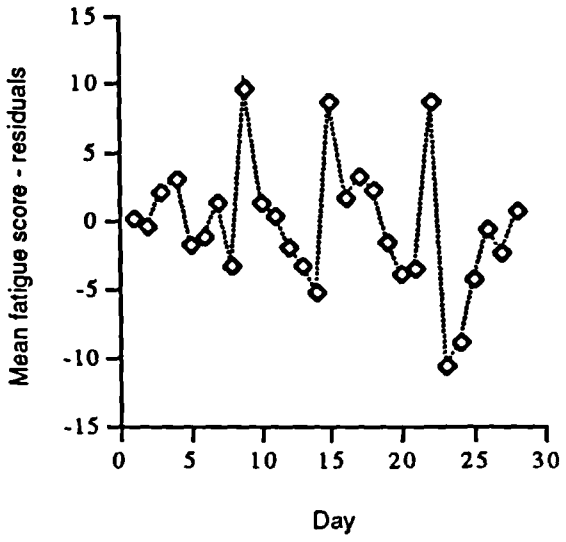
b)

```
                                  acf
              -1.0 -0.8 -0.6 -0.4 -0.2  0.0  0.2  0.4  0.6  0.8  1.0
              +----+----+----+----+----+----+----+----+----+----+----+
     1  -0.079                         XXX
     2  -0.175                       XXXXX
     3   0.101                           XXXX
     4   0.047                           XX
     5   0.121                           XXXX
     6  -0.070                         XXX
     7   0.023                           XX
lag  8   0.213                           XXXXXX
     9  -0.176                       XXXXX
    10  -0.110                        XXXX
    11  -0.099                        XXX
    12  -0.033                         XX
    13   0.076                           XXX
    14  -0.078                         XXX
```

The analysis was repeated with the data derived from subjects receiving a weekly cycle of chemotherapy with the slight changes to the specifications. The ARIMA command within Minitab confirmed that the models described above gave a fair representation of the data sets for mean fatigue score and concentration. The residuals and the Modified Box-Pierce chi-square statistic indicated that the models chosen were satisfactory on statistical grounds (see figure 6.16 and 6.18).

Figure 6.21 a) Residuals from fitting a seasonal AR(1) model to the *mean fatigue score* weekly series and b) the correlogram of the residuals

a)



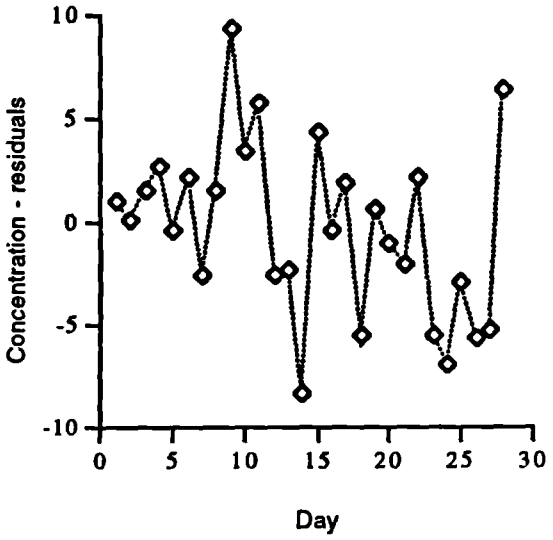
b)

```
                                    acf

          -1.0 -0.8 -0.6 -0.4 -0.2  0.0  0.2  0.4  0.6  0.8  1.0
            +----+----+----+----+----+----+----+----+----+----+----+
     1   0.017                          X
     2  -0.029                         XX
     3  -0.056                         XX
     4  -0.028                         XX
     5  -0.079                        XXX
     6   0.181                          XXXXXX
     7   0.092                          XXX
Lag  8  -0.167                       XXXXX
     9  -0.110                        XXXX
    10  -0.074                         XXX
    11   0.081                          XXX
    12   0.029                          XX
    13   0.190                          XXXXXX
    14  -0.212                      XXXXXX
    15  -0.065                         XXX
```

Figures 6.21 and 6.22 depict visual representations of the residuals remaining when fitting the chosen model, an AR(1) model with a 7-day seasonal element in the case of the weekly *mean fatigue score* series and a 7-day seasonal model in the case of the weekly *concentration* series. In both cases the residuals remain relatively low and there is no obvious pattern, but there are some large values. This was reflected in the degree of fit achieved, and only moderate t-ratios were obtained when fitting the selected models.

Figure 6.22 a) Residuals from fitting a seasonal model to the weekly *concentration* series and b) the correlogram of the residuals

a)



b)

```
                                  acf
          -1.0 -0.8 -0.6 -0.4 -0.2  0.0  0.2  0.4  0.6  0.8  1.0
           +----+----+----+----+----+----+----+----+----+----+----+
     1   0.140                          XXXX
     2   0.167                          XXXXX
     3  -0.085                        XXX
     4  -0.060                        XXX
     5  -0.049                         XX
     6   0.260                           XXXXXXXX
     7   0.084                          XXX
Lag  8  -0.063                        XXX
     9  -0.016                          X
    10  -0.084                        XXX
    11   0.109                          XXXX
    12  -0.031                         XX
    13   0.105                          XXXX
    14  -0.250                    XXXXXXX
    15  -0.275                    XXXXXXXX
```

6.7 Summary

This chapter has outlined a) the nature of the sample and quality of data obtained in the study and b) the findings of visual and statistical analyses used to generate a description of the patterns of fatigue which occur following the administration of chemotherapy.

The individual vignettes illuminate the diverse experiences and characteristics of patients who receive chemotherapy. They illustrate the value of reflecting on the circumstances of each subject during the period of data collection when interpreting

patterns which emerge from the diary data in relation to fatigue, other symptoms and aspects of mood.

The sample was varied and this combined with sample attrition limits the extent to which conclusions can be made concerning the typicality of the patterns in fatigue which were noted following the administration of the various chemotherapy protocols. Visual analysis of the *mean fatigue* plots related to the *type of chemotherapy* facilitated the identification of a number of themes : mirror/parallel shifts, large declines and improvements, stability versus dynamism and dynamics at the start, middle and end of diary keeping.

Alternatively subjects were divided according to the nature of chemotherapy delivery rather than according to the individual protocol (resulting in relatively robust sub-groups). Three distinct trajectories emerged from the relevant time plots. The features of these data have been described and illustrated with reference to a selection of time plots and by fitting ARIMA models to the various series. Essentially this latter procedure was acheived by fitting a number of different models and then examining how well they fitted. Models which gave the "best" fit were chosen to provide explanations of these data. An AR(1) model gave the best representation of the observed time series for both the 21-day and 28-day *mean fatigue score* series, whereas an AR(1) model with a 7-day seasonal element was most appropriate to explain the behaviour of the weekly chemotherapy series.

CHAPTER 7

RESULTS II

7.1 Introduction

This chapter reports the results derived from analysis of the aggregated data set. It complements Chapter 6 which examined data for the presence of visual patterns from a standpoint of individual and grouped data sets, supported by a time series analysis. Statistics can provide insight into the pattern of change and differences between groups. Hence, the richness of the individual daily data has to be sacrificed for the sake of compact, objective summaries. Scores achieved on the daily diary items will be reported, correlated and compared for differences between groups. Finally, the pattern and nature of *self-care* behaviour in response to fatigue will be summarised

7.2 Aggregated Scores For Daily Diary Items

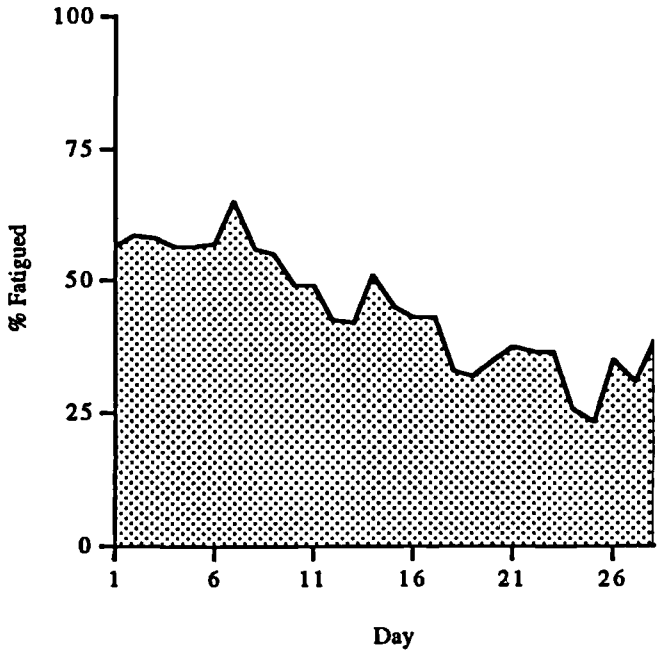
The diary contained a number of discrete parts. The first part consisted of six visual analogue scales exploring various aspects of *mood, appetite, nausea* and *sleep.* The second part comprised four visual analogue scales representing the various dimensions of fatigue, checked boxes to confirm the presence or absence of fatigue at specific times of the day, a record for patients to document *self-care* behaviours and their effectiveness and a few open-ended items to elicit views on the contributory causes of their fatigue and any other symptoms experienced during the day. Section 7.2 details the results in relation to the aggregated data set concerning the percentage of subjects reporting fatigue, the various scores achieved on the visual analogue scales, and the periods of the day when fatigue was reported to be present. In addition, opinions about the causes of fatigue and the presence of other symptoms on a day to day basis will be reported.

7.2.1 Percentage of subjects reporting fatigued

Just under 90% (88.9% , 98) of the sample reported fatigue at some point during the diary keeping period: only 11 subjects failed to report any fatigue on any of the diary days. Figure 7.1 provides a graphical representation of the percentage of subjects who

experienced fatigue on a daily basis over the diary keeping period. They recorded whether they were fatigued or not on 2,259 diary days. During 46.8% of these days (1,057 diary days), subjects experienced some degree of fatigue at some point during the day.

Figure 7.1 Percentage of subjects experiencing fatigue on a daily basis



During the final interview subjects were asked to reflect on whether they felt fatigue had significantly altered during diary keeping compared with any previous experiences. Responses were categorised according to whether subjects felt fatigue had worsened (36, 35.6%), reduced (22, 21.8%) or stayed the same (43, 42.6%). When subjects were asked to provide a reason(s) why fatigue may have worsened or improved a wide range of responses were obtained. These have been coded into categories using the framework provided by Piper (1989). They are summarised in table 7.1. A further 4 subjects stated that worsening fatigue was caused by a combination of circumstances and one subject was unable to offer reasons. Similarly, 3 subjects could not offer a reason for their reduced fatigue.

Futhermore, when the responses of subjects completing their first pulse of chemotherapy were analysed (26) as a sub sample, 63.2% of them recounted worsening fatigue following the delivery of chemotherapy. However, 36.8% reported their fatigue to be unchanged. None of this sub sample felt their fatigue had abated. These subjects most commonly perceived this increase in fatigue to be due to the treatment.

Table 7.1 Perceived causes of improved or worsened fatigue during diary keeping period reported during final interview

Perceived cause of improved or worsened fatigue	Examples : worsened	Percentage of responses within sub category (n=36)*	Examples : improvement	Percentage of responses within sub category (n=22)*
Treatment patterns	Chemotherapy Radiotherapy Stopped steroids	47.2% (17)	Stopped radiotherapy Chemotherapy	22.7% (5)
Other patterns	Symptoms (breathlessness, pain) Nutrition Environment (the weather) Innate host factors i.e. old age	33.3% (12)	Symptoms decreased Environment (the weather)	27.3% (6)
Activity/rest patterns	Excessive work demands Visiting/waiting at hospital for tests	11.1% (4)	Increased help around the house Holiday Preventative rest	9.1% (2)
Disease patterns	Co-existing illness	8.3% (3)	Cancer - disease regression	18.2% (4)
Sleep/wake patterns	Lack of sleep	8.3% (3)		
Psychological patterns	Boredom Anxiety Expectation of fatigue	5.5% (2)	Doing more and thus not as bored Increased motivation and better mood Know this is the final treatment	27.3% (6)

*Subjects could respond more than once thus figures do not add up to 100%

7.2.2 Perceived causes of fatigue

On the days when subjects had indicated that they had experienced fatigue, they were asked to remark on their perception of what contributed to or caused the fatigue. A variety of responses were obtained, coded as above and are displayed in table 7.2. Subjects often gave more than one response or failed to respond to this item.

Table 7.2 Perceived causes of fatigue recorded in diary

Perceived cause of fatigue and percentage of subjects reporting*	Sub-categories	Number of responses within sub-category
Treatment patterns	Chemotherapy	458
	Medical -related to sequelae	79
47.4%	of chemotherapy and/or disease	
	Radiotherapy	13
Activity/rest patterns	Work and multiple social demands	106
15.9%	Everyday activities	40
	Visiting/waiting at hospital	38
Other patterns	Symptoms	123
	Nutrition	20
14.3%	Environment	20
	Innate host factors i.e. old age	3
Disease patterns	Cancer	97
9.1%	Co-existing illness	9
Sleep/wake patterns	Lack/change in sleep	100
8.6%	pattern	
Psychological patterns	Anxiety and worry with emotional upset	17
2%	Boredom	6

*2.76% Stated "not sure" or "nothing in particular"

Fatigue was attributed most commonly to the chemotherapy treatment. A variety of symptoms featured prominently within the "Other Patterns" category, including bowel and stomach disturbances (26 responses), pain (32 responses) and nausea (8 responses).

7.2.3 Presence of symptoms

Comments were elicited concerning other symptoms or problems experienced on the same days as fatigue. When subjects completed this item (1,009 occasions out of a possible 2,259 diary days), half of the time they recorded the presence of additional noteworthy symptoms. Responses to this question are to be found in table 7.3. They have been categorised with examples given for each, to reflect the framework of Carrieri-Kohlman, Lindsey and West's (1993) for organising pathophysiological clinical patient problems. All are human responses to illness, some are symptoms and some are processes.

Table 7.3 Nature of additional symptoms/problems recorded in daily diary on days when subjects recorded the presence of fatigue

Symptom category	% experienced (number of episodes recorded)
Alterations in sensation e.g. dyspnoea, pain, altered taste and/or smell, paresthesia, itching	63.1 (469)
Alterations in regulation e.g. palpitations, anorexia, lack of concentration, thrombosis, increased temperature, shivering	18.2 (135)
Alterations in protection e.g. impaired sleep, hair loss, low white count. influenza/cold, stress responses	13.3 (99)
Alterations in motion e.g. muscle cramp, shakiness, weakness	5.4 (40)

Subjects sometimes recorded more than one symptom. The most common category constituted alterations in sensation. The most common inclusions within this category were complaints about a peculiar taste or smell, paresthesia and problems with vision. In this subsample of observations a Mann-Whitney test revealed that greater *mean fatigue scores* were recorded when the subject indicated they experienced additional symptoms/problems (U =101,138, p =<.01).

Subjects responded to an item concerned with alterations in their health or whether during the diary keeping their health had remained constant. Those who considered this was not the case reported a variety of problems which most commonly included a period of neutropenia and resulting infection (11), multiple problems associated with treatment (7) and gastrointestinal problems such as diarrhoea (9). A Mann-Whitney test revealed a significant relationship between the report of a change in health and resulting additional problems and a greater respondent *mean fatigue score* (U =779, p =<.01).

7.2.4 Period of the day when fatigue was reported

Subjects who experienced fatigue were asked to indicate the times of day when they felt fatigued. The late afternoon to late evening period seemed to be more problematic than the early morning to early afternoon period. The data in table 7.4 confirmed this. The

early afternoon, late afternoon and early evening appear to be the periods of day when the subjects were most likely to experience fatigue; 53.3% (557 recordings), 58.1% (608 recordings) and 57.3% (599 recordings) respectively.

Table 7.4 Number of observations when subjects indicate they are fatigued at a particular period of the day

	Period of day					
	Early morning	Late morning	Early afternoon	Late afternoon	Early evening	Late evening
Fatigued	328 (31.4%)	397 (38.0%)	557 (53.2%)	608 (58.1%)	599 (57.3%)	470 (44.9%)
Not fatigued	718 (68.6%)	649 (62.0%)	489 (46.8%)	438 (41.9%)	447 (42.7%)	576 (55.1%)

Chi-Square tests (χ^2) for two independent samples were performed to discern whether fatigue experienced at one time period was related to fatigue experienced at another. The results are presented in table 7.5. This suggested that subjects who were fatigued during one period of the day were more likely to be fatigued during an adjacent period of the same day. There appeared to be a correspondence between those who experienced fatigue, for example, during the early afternoon and those who experienced fatigue in the late afternoon. The non-significant results tended to relate to periods of the day which were not temporally adjacent to each other.

Table 7.5 Results of chi-square tests examining associations between fatigue experienced at one time in the day with fatigue experienced at another point in the day

	Early morning	Late morning	Early afternoon	Late afternoon	Early evening
Late morning	157.9***				
Early afternoon	23.4***	95.7***			
Late afternoon	N.S	9.0**	8.5**		
Early evening	N.S	N.S	6.3*	59.4***	
Late evening	55.5***	4 .00*	N.S	30.5***	79.3***

N.B. *χ^2 Significant at 5%; ** χ^2 Significant at 1%; * **χ^2 Significant at .1%.

To examine whether there was any association between the number of time periods a subject indicated they were fatigued and the *mean fatigue score*, a Kruskal-Wallis test was performed. The result was as follows:

Mean fatigue score H = 362.7 5 *df* p =<.01

On examining the medians it appeared that the *mean fatigue score* was greater in those who were tired for a larger proportion of the day. For subjects who experienced fatigue during only one period of the day this resulted in a median of 24.5 (mean rank 294) whereas subjects who indicated they experienced fatigue during three of the specified time periods recorded a median of 51.1 (mean rank 583). Finally, those who were fatigued for the entire day scored a median of 79.8 (mean rank 865).

7.2.5 Mean scores of daily diary items

Table 7.6 depicts the respondent and overall mean scores and standard deviations of items recorded in the daily diary for the combined data set. The respondent means ranged from 18.2 (SD 17.2) for *nausea* to 33.0 (SD 19.1) for the *happy - sad* bipolar visual analogue scale. Similarly, the overall means ranged from 16.4 (SD 22.2) for *nausea* to 31.6 (SD 24.2) for the *happy - sad* bipolar visual analogue scale. The visual analogue scales concerned with fatigue ranged from 26.8 for *extent of fatigue* to 18.6 for *distress from fatigue* with a respondent *mean fatigue score* computed from the four fatigue VASs of 23.5. The overall mean and the respondent mean should be approximate when each individual has an equal number of diary days. When this is not so, the overall mean will give more weight to those individuals who have completed a greater percentage of the diary. The respondent mean, otherwise known as the mean of means gives equal weight to each subject. Both values were computed to determine whether there was any difference between them and its magnitude. For example, in table 7.6 the respondent *mean extent of fatigue score* was 26.8 and the corresponding overall mean was 25.3. In the tables 7.7–7.9 the respondent mean is reported as inspection of values revealed negligible differences between the two.

Table 7.6 Mean scores of items in the daily diary

Items in daily diary	Respondents' Mean (average of the person-based means n =109)	SD	Overall Mean (average across diary days)	SD
Calm-Anxious	29.6	19.7	28.5	26.1
Happy-Sad	33.0	19.1	31.6	24.2
Inability to concentrate	32.0	18.7	30.5	25.0
Appetite	26.6	21.8	23.6	26.1
Sleep	33.0	20.4	31.4	27.4
Nausea	18.2	17.2	16.4	22.2
Extent of fatigue	26.8	23.7	25.3	32.2
Distress from fatigue	18.6	20.4	17.1	26.4
Fatigue interfered with ability to carry out daily activities	23.7	23.1	22.1	31.1
Fatigue prevented subjects from doing things that are enjoyed	24.4	23.7	22.8	32.3
Mean fatigue score	23.5	22.0	21.9	29.0

Table 7.7 describes the mean scores for items in the daily diary according to the nature of chemotherapy cycle the subjects were receiving. The *mean fatigue scores* for the 21-day, 28-day and weekly cycle were 25.9 (SD 23.2), 18.8 (SD 16.1) and 23.1 (SD 26.4) respectively. To determine whether these findings were significant a Kruskal-Wallis test was performed and revealed the following :

Mean fatigue score H = 6.5 2 *df* p <.05

By considering the mean ranks of the different groups, it was apparent that those subjects receiving a 21-day regime were significantly more fatigued than those undergoing either a 28-day or weekly regime; the mean ranks were 1,163, 1,092 and 1,115 respectively.

Table 7.7 Mean scores of items in daily diary for subjects receiving a 21-day cycle, 28-day cycle and weekly cycle

Items in daily diary	21-day cycle (n=61)		28-day cycle (n=31)		Weekly cycle (n=17)	
	Mean	SD	Mean	SD	Mean	SD
Calm-Anxious	31.4	20.5	28.3	17.4	25.5	21.1
Happy-Sad	35.1	20.2	30.1	16.9	30.6	18.9
Inability to concentrate	34.0	17.1	27.5	17.9	32.6	24.4
Appetite	29.5	21.6	17.2	16.4	33.3	26.5
Sleep	35.8	21.3	28.6	16.9	30.5	22.2
Nausea	19.0	17.5	14.3	13.5	22.2	21.4
Extent of fatigue	29.1	25.3	23.7	19.1	24.2	25.9
Distress from fatigue	21.2	21.9	13.7	14.2	18.0	23.7
Interference with ability to carry out daily activities	25.9	23.9	18.8	17.5	24.6	28.6
Prevented from doing things that are enjoyed	27.0	25.2	18.7	16.1	25.5	29.0
Mean fatigue score	25.9	23.2	18.8	16.1	23.1	26.4

Tables 7.8–7.9 depict the aggregated mean and standard deviation over a number of discrete 7-day time periods for the diary variables in relation to a particular type of chemotherapy cycle. In the case of the 28-day and 21-day cycle these time periods were chosen as they reflected the first week following chemotherapy (days 1–7), the time leading up to the potential nadir (days 8–14) and the period prior to the next pulse of treatment (days 15–21 and 22–28 if applicable). In the case of the weekly cycle the time periods corresponded to each week following a pulse of chemotherapy.

Table 7.8 Mean scores of daily diary items at different time periods and results of RM-ANOVA for subjects receiving a 21-day cycle (n=61)

Items in daily diary	Day 1–7		Day 8–14		Day 15–21		RM-ANOVA	
	Mean	SD	Mean	SD	Mean	SD	F value	p
Calm-Anxious	34.4	21.0	28.8	21.2	25.8	19.5	7.5	<.01
Happy-Sad	37.3	18.8	34.3	21.5	28.4	20.5	8.1	<.01
Inability to concentrate	35.1	18.2	35.2	20.5	27.5	17.5	5.5	<.01
Appetite	32.2	22.3	25.8	20.8	20.0	19.3	5.3	<.01
Sleep	41.0	23.0	34.0	22.0	25.3	20.4	10.9	<.01
Nausea	22.3	19.4	16.2	16.8	11.7	13.4	6.8	<.01
Extent of fatigue	33.1	26.5	28.2	28.3	18.2	23.9	7.7	<.01
Distress from fatigue	23.1	22.0	20.4	23.7	14.2	20.0	4.9	<.05
Interference with ability to carry out daily activities	29.2	24.8	25.4	27.5	17.4	23.0	7.8	<.01
Prevented from doing things that are enjoyed	30.5	26.6	27.4	29.8	18.4	23.5	10.0	<.01
Mean fatigue score	29.3	23.7	25.5	26.5	17.0	22.2	8.6	<.01

N.B. In all RM-ANOVA $df_1 = 2$ and $df_2 = 42$.

In those subjects receiving a 21-day cycle (table 6.5) there appeared to be a gradual decline in the aggregated *mean fatigue score* over the 3 different time periods : 29.3 (SD 23.7), 25.5 (SD 26.5), 17.0 (SD 22.2) over days 1–7, days 8–14 and days 15–21 respectively. This is a trend which was repeated with all of the other variables.

Table 7.9 Mean scores of daily diary items at different time periods and results of RM-ANOVA for subjects receiving a 28-day cycle (n=31)

Items in daily diary	Day 1–7		Day 8–14		Day 15–21		Day 22–28		RM-ANOVA	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F value	p
Calm-Anxious	33.9	21.2	31.5	22.3	25.9	21.1	24.4	20.4	2.3	N.S.
Happy-Sad	35.5	18.2	31.9	19.0	28.4	20.1	27.6	21.1	2.2	N.S
Inability to concentrate	35.1	21.2	29.4	20.3	24.7	19.2	23.2	20.5	7.1	<.01
Appetite	25.3	21.2	18.2	20.6	13.8	16.8	12.4	18.4	5.1	<.01
Sleep	35.0	18.3	30.2	20.6	26.2	21.4	24.0	21.4	3.6	<.05
Nausea	22.9	22.3	15.2	19.2	11.0	14.0	8.9	14.4	3.4	<.05
Extent of fatigue	36.0	23.0	26.3	23.9	19.3	21.9	15.7	21.3	8.2	<.01
Distress from fatigue	20.8	16.5	17.6	20.3	10.0	15.8	8.2	15.5	6.7	<.01
Interference with ability to carry out daily activities	30.1	22.3	21.5	23.9	14.3	18.1	11.4	20.8	6.0	<.01
Prevented from doing things that are enjoyed	30.0	22.1	21.8	22.9	13.8	17.1	11.2	19.1	6.0	<.01
Mean fatigue score	29.3	19.6	22.0	22.1	14.4	17.5	11.6	18.6	7.3	<.01

N.B. In all RM-ANOVA $df_1 = 3$ and $df_2 = 27$.

Similarly during the 28-day cycle (table 7.9) there was a decline in the *mean fatigue score* over each of the four time periods ; 29.3 (SD 19.6), 21.9 (SD 22.1), 14.4 (SD 17.5) and 11.6 (SD 18.6) over days 1–7, days 8–14 and days 15–21 and days 22–28 respectively. Again this trend was repeated with all of the other variables. With the addition of an extra seven days prior to the next pulse of chemotherapy, the *mean fatigue score* for the 28-day cycle reached only 11.6 over days 22–28 in contrast to 17.0 over days 15–21 for the 21-day cycle.

Table 7.10 Mean scores of daily diary items at different time periods for subjects receiving a weekly cycle (n=17)

Items in daily diary	Day 1–7		Day 8–14		Day 15–21		Day 22–28	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Calm-Anxious	23.7	20.6	26.0	22.8	28.1	26.9	23.5	22.5
Happy-Sad	30.1	18.8	30.1	19.6	30.4	23.6	27.9	19.1
Inability to concentrate	31.1	25.8	31.7	22.9	31.4	27.8	27.9	21.3
Appetite	31.5	24.6	32.3	27.5	34.3	32.4	30.9	26.8
Sleep	30.5	20.7	33.3	23.6	30.0	25.7	32.6	26.3
Nausea	23.3	23.3	18.4	16.7	18.8	18.3	16.9	15.9
Extent of fatigue	24.8	25.8	27.7	30.6	25.8	29.5	18.2	19.0
Distress from fatigue	16.7	20.3	20.0	26.7	21.0	29.5	15.1	22.2
Interference with ability to carry out daily activities	24.7	27.9	25.3	31.2	25.4	31.7	18.2	23.1
Prevented from doing things that are enjoyed	26.3	27.5	25.7	30.7	25.8	32.7	19.1	24.2
Mean fatigue score	23.1	24.7	24.7	29.3	24.5	30.48	17.7	21.9

With a weekly cycle of administration (table 7.10) the *mean fatigue score* remained relatively similar over each 7-day time period, 23.1 (SD 24.7), 24.7 (SD 29.3), 24.5 (SD 30.5) and 17.7 (SD 22.0 $p<.05$) over days 1–7, days 8–14 and days 15–21 and days 22–28 respectively. This pattern was reflected in the other daily VASs.

Employing RM-ANOVA facilitated a more precise examination of the influence of time, recognising time within-subjects as a factor. This technique compares a number of observations simultaneously. However, RM-ANOVA requires interval level data while the data derived from the repeated measures in the current study were not at this level. This difficulty was overcome by ranking the original data and using ranks in the computation of test statistics. The results for the 28-day cycle examining the effect of time within subjects can be found in table 7.9. Decline in all scores except *Happy-Sad* and *Calm-Anxious* achieved significance, at the $p<.05$ level . Likewise, the results for

the 21-day cycle can be found in table 7.8, and in this cycle all variables achieved a significant *F* value. The relatively stable scores for all variables in those receiving a weekly cycle resulted in non-significant *F* values for all variables.

7.3 Analysis Of Group Differences In Fatigue Scores By Demographic Variable

A principal aim of the study, in addition to monitoring the subjective dimensions of fatigue, was to describe the nature of the relationship between factors which may influence it. This section explores differences in *mean fatigue scores* in relation to subjects' sociodemographic and medical characteristics. Results concerned with mood and symptom distress, measured with the Mood Adjective Checklist and Holmes Symptom Distress Scale respectively, appear in Chapter 8.

The Kruskal-Wallis test statistic was employed to detect significant differences in the respondent *fatigue scores* in relation to demographic variables. Subjects receiving CHLVPP, EPIC, PMB, continuous 5-Fu and VEEP were omitted when analysing the results concerned with *type of chemotherapy*. Non-Hodgkin's and Hodgkin's lymphoma subjects and pancreatic and cholangiocarcinoma subjects were combined, and subjects with cervical cancer were omitted when analysing the results concerned with *site of cancer*. Within the *nature of administration* group those receiving continuous chemotherapy were omitted. These manipulations were necessary due to small sample size. A rough approximation concerning the number of subjects in each sub-set can be obtained by referring to table 6.2 in Chapter 6. When presenting the results in the following sections the figures in brackets represent the median value and mean rank respectively.

7.3.1 Extent of fatigue

The significant results for the VAS concerned with *extent of fatigue* by selected demographic and medical variables were as follows:

Site of cancer	H = 19.1	7 *df*	$p = <.01$
Type of chemotherapy	H = 19.7	7 *df*	$p = <.01$
Nature of administration	H = 5.8	2 *df*	$p = <.05$

In relation to *site of cancer, extent of fatigue* was greater in those with a cholangiocarcinoma or pancreatic cancer (56.8, 78), breast cancer (31.6, 74) or a lymphoma (32.2, 67) and lowest in those with an unknown primary (7.0, 34) or small cell lung cancer (7.3, 40). Within *type of chemotherapy* those subjects receiving weekly 5-Fu or ECF held the highest medians, 36.8 (mean rank 61) and 36.5 (mean rank 65) respectively, and those receiving Cisplatin and 5-Fu and Epirubicin and Etoposide the lowest, 4.4 (mean rank 28) and 7.3 (mean rank 38) respectively. The combination of the bolus and continuous *method of administration* resulted in a median of 36.5 (mean rank 69) in contrast to a median of 16.7 (mean rank 52) in subjects receiving bolus and/or short term infusions.

7.3.2 Distress from fatigue

The significant results for the VAS concerned with *distress from fatigue* by selected demographic and medical variables were as follows:

Type of chemotherapy	H = 13.6	7 *df*	$p = <.05$
Nature of administration	H = 6.4	2 *df*	$p = <.05$

In relation to *type of chemotherapy* , *distress from fatigue* was greater in those receiving CMF, ECF or weekly 5-Fu : achieving median values of 20.1 (mean rank 61), 17.9 (mean rank 65) and 12.7 (mean rank 57) respectively in contrast to those receiving Cisplatin and 5-Fu (3.6, 34). The combination of the bolus and continuous *method of administration* resulted in a median of 17.9 (mean rank 69) in contrast to a median of 4.9 (mean rank 45) in subjects receiving weekly bolus injections of chemotherapy.

7.3.3 Interference with ability to carry out daily activities/chores

The significant results for the VAS concerned with the degree to which *fatigue interfered with performance of daily activities/chores* by selected demographic and medical variables were as follows:

Site of cancer	H = 18.6	7 *df*	$p = <.01$
Type of chemotherapy	H = 22.1	7 *df*	$p = <.01$
Nature of administration	H = 7.4	2 *df*	$p = <.05$

In relation to *site of cancer*, on examining the medians the degree to which *fatigue interfered with the performance of daily activities/chores* was greater in those with a cholangiocarcinoma or pancreatic cancer (41.0, 79), breast cancer (23.1, 68), or a lymphoma (20.0, 65) in contrast to subjects with an unknown primary (1.9, 29) or small cell lung cancer (5.3, 41). Within *type of chemotherapy* , those subjects receiving weekly 5-Fu, CMF or ECF held the highest medians, 43 (mean rank 66), 27.25 (mean rank 64) and 28.33 (mean rank 67) respectively. The combination of bolus and continuous *method of administration* resulted in a median of 28.3 (mean rank 71) in contrast to a median of 11 (mean rank 51) in subjects receiving bolus and/or short term infusions.

7.3.4 Fatigue preventing subjects from doing things they enjoyed

The significant results for the VAS concerned with the degree to which *fatigue interfered with subjects engaging in activities they enjoyed* by selected demographic and medical variables were as follows:

Site of cancer	H = 18.6	7 *df*	$p = <.01$
Type of chemotherapy	H = 22.1	7 *df*	$p = <.01$
Nature of administration	H = 8.0	2 *df*	$p = <.01$

In relation to *site of cancer* the degree to which *fatigue interfered with the subject engaging in activities they enjoyed* was greater in those with a cholangiocarcinoma or pancreatic cancer (41.0, 79) and those with breast cancer (23.1, 68) in contrast to subjects with an unknown primary (1.9, 29). Within *type of chemotherapy,* those subjects receiving weekly 5-Fu, ECF or CMF held the highest medians, 41.7 (mean rank 65), 24.4 (mean rank 68) and 23.1 (mean rank 64) respectively. Those receiving Cisplatin and 5-Fu attained a median value of 1.0 (mean rank 24). The combination of the bolus and continuous *method of administration* resulted in a median of 24.4 (mean rank 72), whereas those receiving bolus and/or short term infusions achieved a median of 15.6 (mean rank 50).

7.3.5 Mean fatigue score

The significant results for the combined VASs, the *mean fatigue score*, by selected demographic and medical variables were as follows:

Site of cancer	H = 17.4	7 *df*	$p = <.05$
Type of chemotherapy	H = 20.2	7 *df*	$p = <.01$
Nature of administration	H = 8.0	2 *df*	$p = <.05$

In relation to *site of cancer* the *mean fatigue score* was greater in those with a cholangiocarcinoma or pancreatic cancer (45.9, 78), breast cancer (23.9, 71) or a lymphoma (23.3, 66) rather than those with an unknown primary (6.6, 36). Within the different *types of chemotherapy* subjects receiving weekly 5-Fu or ECF attained the highest medians, 29.2 (mean rank 64) and 28.3 (mean rank 66) respectively, in contrast to those receiving Cisplatin and 5-Fu (4.0, 30). The combination of bolus and continuous *method of administration* resulted in a median of 28.3 (mean rank 70), whereas those receiving weekly bolus injections of drugs achieved a median of 10.6 (mean rank 49).

There were no significant findings when the respondent mean fatigue scores recorded during diary keeping were examined for any association with the presence of additional health problems and the severity of such health problems (ascertained at interview) using the Kruskal-Wallis test statistic. Likewise, there was no significant association between respondent mean fatigue scores for those subjects who lived on their own as opposed to with others. No significant differences were revealed between those who worked or did not work during diary keeping. When respondent *mean fatigue scores* were examined as to whether subjects perceived they had experienced a change in their level of independence over the diary keeping period, a Kruskal-Wallis procedure revealed no significant differences between the groups.

7.3.6 Box plots

Box plots are frequently recommended as a valuable alternative method of examining the data during exploratory data analysis. The box plot displays the distribution of scores in the form of a rectangle, between the upper and lower quartiles with projections to the largest and smallest observations. The median is also marked. Box plots are particularly useful for comparing location and variability between several groups (Chatfield, 1988). Figures 7.2 through 7.7 depict box plots for selected demographic variables and fatigue

Figure 7.2 Box plots of mean fatigue scores by type of chemotherapy

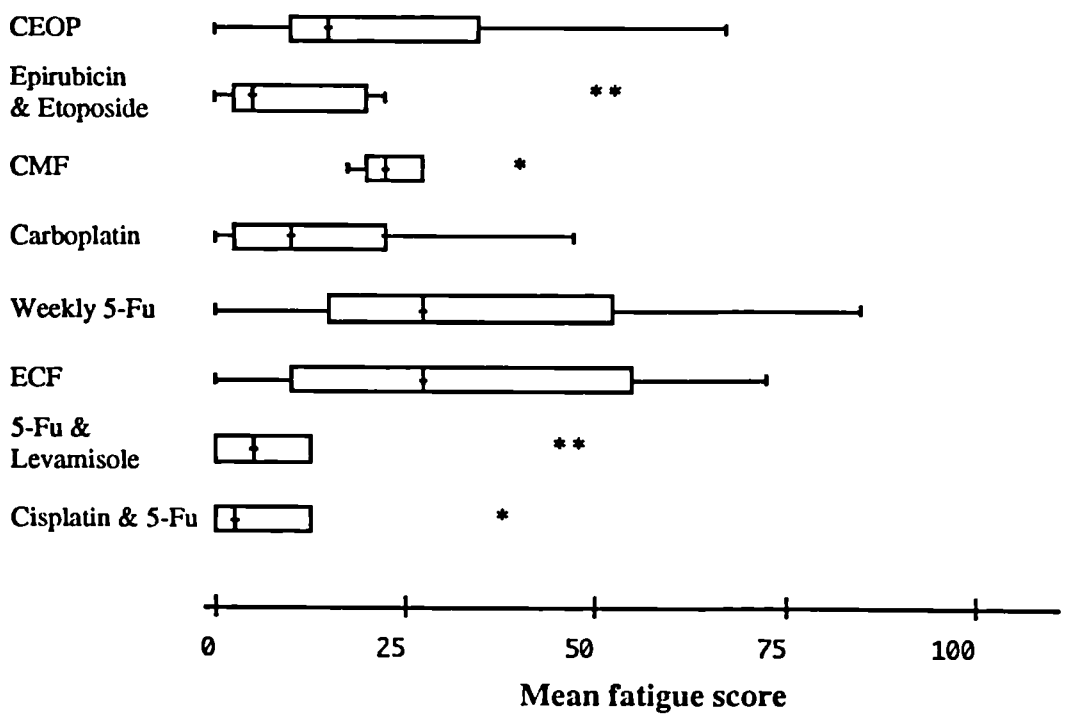
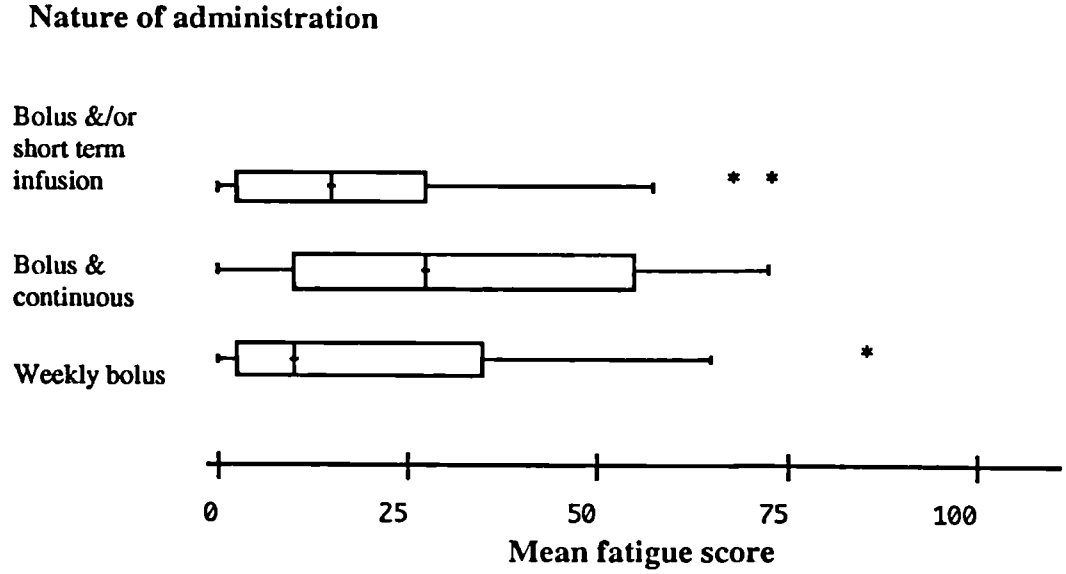
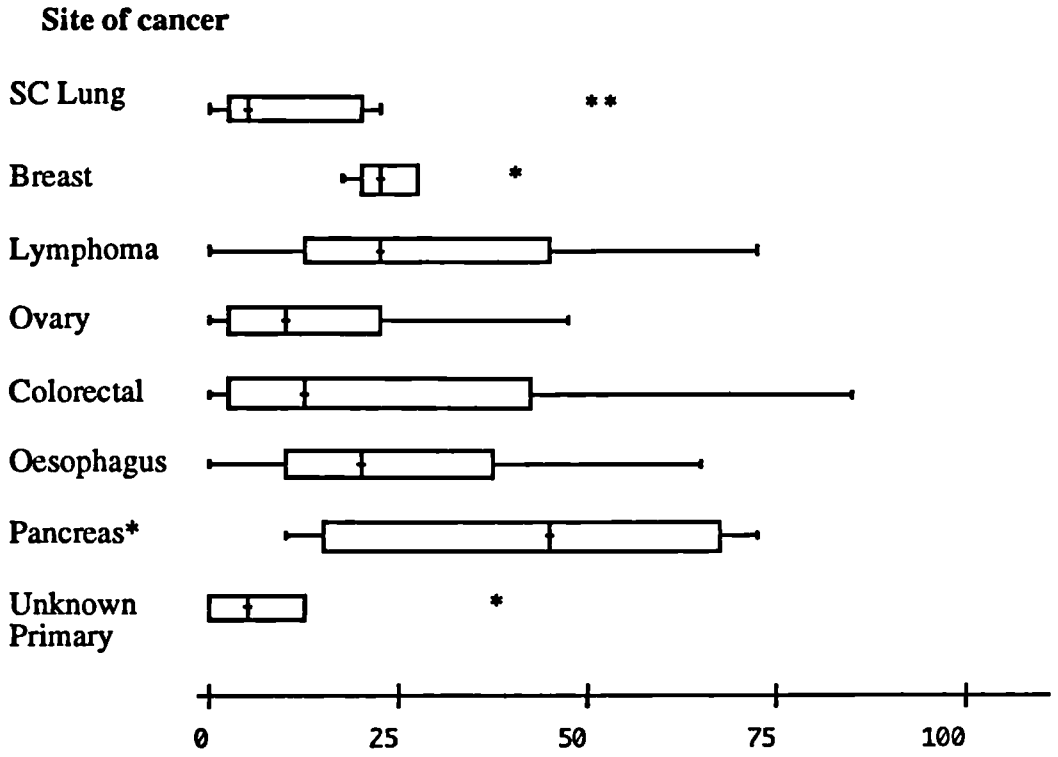


Figure 7.3 Box plots of *mean fatigue scores* by *nature of administration* of chemotherapy



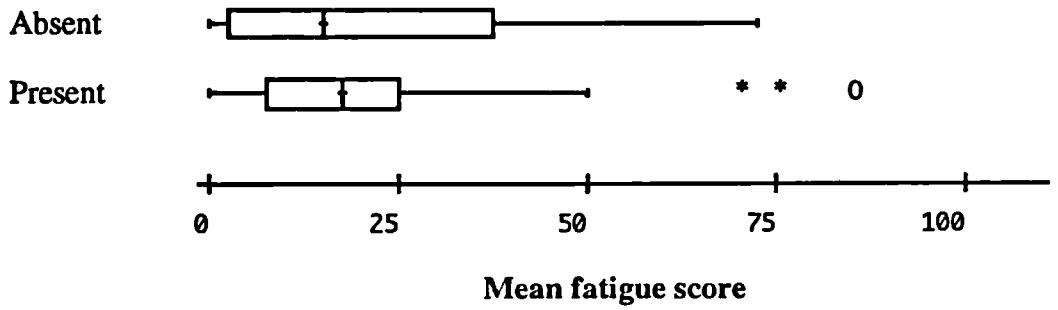
scores confirming results detailed above. In these figures the median of the data is marked with a "+". The left "I" is the lower hinge (essentially the first quartile) and the right "I" is the upper hinge (essentaily the third quartile). Thus the "box" represents the middle half of the data. Possible outliers are plotted with an "*", and probable outliers with a "0".

Figure 7.4 Box plots of scores indicating *mean fatigue scores* by *site of cancer*



N.B Pancreas* includes subjects with a cholangiocarcinoma

Figure 7.5 Box plots of *mean fatigue scores* by *presence of liver metastases*



The remaining visual analogue scales from the diary were examined for the presence of statistically significant results in relation to the demographic variables. Due to the large number of variables which were examined only those associations where $p \leq .01$ were considered worthy of comment in this exploratory analysis. The following were found to be significant:

Site of cancer and *appetite*
H = 17.9 7 *df* $p = <.01$
Type of chemotherapy and *appetite*
H = 17.6 7 *df* $p = .01$
Type of chemotherapy and *sleep*
H = 18.4 1 *df* $p = .01$
Nature of administration and *appetite*
H = 811.3 2 *df* $p = <.01$

In relation to *site of cancer,* it appeared that disruptions of *appetite* were greater in those with a cholangiocarcinoma or pancreatic cancer (36.2, 80) and lowest in those with an ovarian cancer (11.1, 38). Within the different *types of chemotherapy,* subjects receiving Cisplatin and 5-Fu and ECF attained the highest medians in relationship to the *lack of appetite* VAS, 42.4 (mean rank 63) and 36.1 (mean rank 67) respectively, in contrast to those receiving Carboplatin (11.1, 34). *Sleep* was more disrupted in those receiving Cisplatin and 5-Fu (42.3, 64) and less so in those receiving 5-Fu weekly (14.0, 24). Subjects receiving chemotherapy via the bolus and continuous *method of administration* achieved a median value of 36.1 (mean rank 74) compared to 15.0 (mean rank 48) in those receiving bolus and/or short-term infusions of chemotherapy in terms of their *lack of appetite.*

7.4 Relationships Between Daily Visual Analogue Scales

Visual analysis has revealed close ties between the fatigue variables and other variables in the diary. When there are changes in one, there is usually a response in another in a parallel direction. This can be further explored and confirmed or refuted statistically by calculating the correlation. The Spearman Rank-Order Correlation Coefficient, r_s, is a measure of the association between two variables. It requires both variables to be measured in at least an ordinal scale so that objects or individuals under study may be ranked in two ordered series (Siegel and Castellan Jr., 1988). This method does not test specifically for linearity but the tendency of y to increase or decrease with x. A correlation matrix was generated for the items in the daily diary (see figure 7.6). Correlation coefficients have been reported to the second decimal place.

Figure 7.6 Correlation matrix derived from the items in the daily diary

2	.83									
3	.72	.74								
4	.41	.44	.52							
5	.38	.39	.36	.38						
6	.33	.32	.38	.61	.37					
7	.41	.44	.45	.32	.24	.20				
8	.46	.47	.49	.36	.26	.24	.95			
9	.42	.45	.48	.34	.24	.22	.95	.96		
10	.40	.44	.47	.34	.23	.22	.95	.95	.98	
11	.43	.46	.49	.35	.24	.22	.98	.98	.99	.98
	1	2	3	4	5	6	7	8	9	10

Key: 1 = Calm-Anxious. 2 = Happy-Sad. 3 = Inability to concentrate. 4 = Appetite.
5 = Sleep. 6 = Nausea. 7 = Extent of fatigue. 8 = Distress from fatigue.
9 = Interference with ability to carry out daily activities.
10 = Prevented from doing things that are enjoyed. 11 = Mean fatigue score.

When as in this case, the sample size was greater than 100, an approximate procedure to decide whether to reject H_0 may be employed, using z as the test statistic ($z = r\sqrt{n-1}$). The α_2 = ½% critical region for testing the tendency of y to increase with x is $r_s \geq .26$ and the α_2 = 5% critical region for testing the tendency of y to increase with x is $r_s \geq .19$. However, in the above correlation matrix there is in excess of 1,000 data points - with such large numbers it is likely that all values will achieve some degree of statistical significance. In this case it is unwise solely to consider the results on the basis of their statistical significance, and useful to debate their clinical significance. It is useful to consider the proportion (percentage) of the variation in y explained by the monotonic relationship with x i.e. r^2.

The values all above .9 are associated with the *fatigue* subscales and the *mean fatigue score* which provide evidence of internal consistency. Strong positive correlations were recorded between the mood items - *sadness*, *anxiety*, and *inability to concentrate*. *Inability to concentrate* and a *poor appetite* appear related (r_s=.52) as do *nausea* and *lack of appetite* (r_s=.61). The other pairs fail to achieve a coefficient above .5 and although significant, only 25% of the variation is explained. Relatively weak

correlations were recorded between the *fatigue* items and the VASs concerned with *nausea* and *sleep.*

7.4.1 Cross correlations

The cross correlation function can be used when there are observations on two time series. The cross correlation function measures the correlation between x_t and y_{t+k}. The correlations in the previous section compare variables on the same day. However, it is possible that fatigue on one day affects the other variables (or fatigue is affected by the other variables) not on that day, but 1 or more days later. Figure 7.7 illustrates the cross correlation function for the two time series *mean fatigue score* and *nausea* for the 21-day cycle, which was similar to the remaining cross correlation functions for the 21-day and 28-day cycle in relationship to *mean fatigue score* and other variables.

Figure 7.7 Cross correlation function and correlelogram - correlates *nausea*(t) and *mean fatigue score* (t+k)

```
          -1.0 -0.8 -0.6 -0.4 -0.2  0.0  0.2  0.4  0.6  0.8  1.0
            +----+----+----+----+----+----+----+----+----+----+
-5    0.110                          XXXX
-4    0.193                          XXXXXX
-3    0.291                          XXXXXXXX
-2    0.409                          XXXXXXXXXXX
-1    0.607                          XXXXXXXXXXXXXXXX
 0    0.821                          XXXXXXXXXXXXXXXXXXXXX
 1    0.759                          XXXXXXXXXXXXXXXXXXX
 2    0.775                          XXXXXXXXXXXXXXXXXXX
 3    0.802                          XXXXXXXXXXXXXXXXXXXX
 4    0.665                          XXXXXXXXXXXXXXXXX
 5    0.501                          XXXXXXXXXXXXXX
```

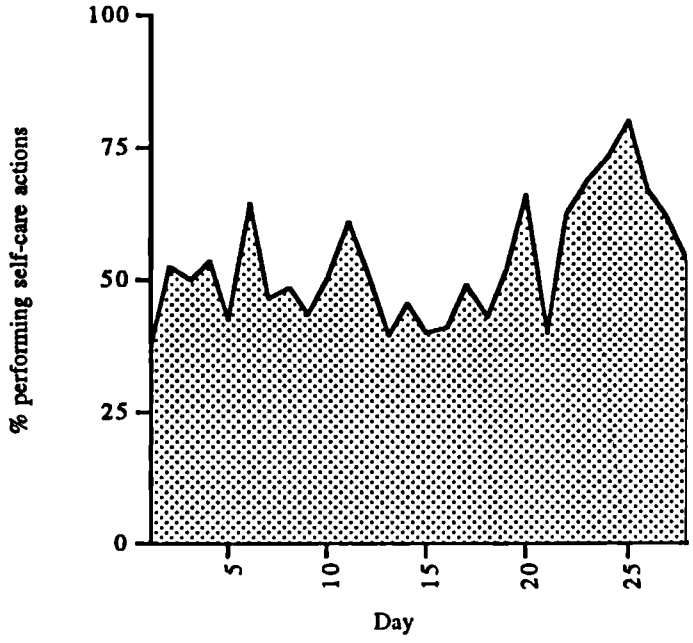
The largest coefficient was obtained with no time lag, with declining values at each successive lag in either direction. This is consistent with an AR(1) series identified through the time series analysis in the preceding chapter. Thus, the relationship between measures is best examined through their values on the same day, as above.

7.5 Self-Care Activity

One of the key areas to be explored in the current study related to self-care. The researcher wished to describe self-care interventions utilised by patients in response to fatigue, and the perceived effectiveness and source of ideas for such interventions. These results will follow.

On the diary days where there was experience of fatigue, *self-care* action initiated with the purpose of relieving fatigue was recorded on approximately half of these occasions (49.9%). Figure 7.8 provides a graphic representation of the performance of *self-care* action on a daily basis. In total 693 separate *self-care* actions were recorded in the diaries. The most frequently recorded number of *self-care* actions was one (80.0%), followed by two (3.9%), three (3.8%) and four actions (2.3%) respectively. Overall, this resulted in a mean of 0.64 *self-care* behaviours for each diary day when fatigue occurred. On only 4 diary days subjects recorded they were fatigued but failed to mark whether they initiated any *self-care* action. In most cases, fatigue was partially relieved (53.7%) by the *self-care action.* In 25.5% of cases it was nearly completely relieved, in contrast to completely relieved (11.5%) or not relieved (9.4%). Subjects failed to record the effectiveness of a particular action on 22 occasions.

Figure 7.8 Percentage of patients performing *self-care* when they are fatigued on a daily basis



There was considerable variation in the nature of *self-care* actions recorded in the diary. Thirty one discrete activities were recorded. Table 7.11 reports the most common activities and the median effectiveness rating for these behaviours. The most commonly used although not the most efficacious *self-care* activity was resting and napping during the day. In addition many subjects read, went for a walk, watched television or retired to bed early.

Table 7.11 Frequency and effectiveness of *self-care* actions of subjects who experienced fatigue

Most frequently recorded self-care actions (number of recordings)	Median effectiveness rating*
Rest/napping during the day (336)	2
Reading (47)	2
Walking (35)	2
Watching television (32)	2
Sleeping for most of the day (31)	2
Went to bed early (28)	3
Undertaking household chores (26)	2
Having a worthwhile conversation (17)	2
Gardening (15)	2
Going to work (14)	2
Engaging in social activities (13)	2

*Effectiveness of self-care actions was recorded on a 4-point scale where 1= not relieved, 2 = partly relieved, 3 = nearly completely relieved and 4 = completely relieved.

When asked to comment on the source of ideas for the *self-care* action subjects most commonly claimed to have the idea themselves (93.6%). Sometimes this was in response to previous experience, common sense or a natural reaction. Other sources of ideas were stated as a family member (2.8%), a nurse (1.4%), a doctor (1.2%) or a friend (1.0%). However, on 197 occasions out of the 693 available to them, subjects failed to complete this item.

Self-care actions were categorised according to whether they fell into a number of groups: modification/alteration in patterns of activity and rest, psychological strategies, attempting to preserve normality, relieving symptoms and providing comfort, social interventions, nutritional strategies and alteration in sleep/waking patterns. The number of subjects employing a type of *self-care* action, the number of actions recorded in each category, and the corresponding median effectiveness rating are displayed in table 7.12.

Table 7.12 Categories of *self-care* behaviours: number of observations and median effectiveness rating

Category of self-care and percentage of subjects employing the action	Self-care strategy	Number of occasions recorded for category	Median effectiveness rating of category
Modification or alteration in activity and rest pattern 83.6%	Rest and napping Taking things easy Modifying activities Walking Gardening	411	2 (range 1–4)
Alteration of sleep-wake pattern 37.0%	Going to bed early Sleeping most of the day	66	2 (range 1–4)
Psychological strategies 24.7%	Listening to relaxation tapes Listening to music Reading Watching television Counselling Homeopathic remedies Acupuncture Relaxation	103	2 (range 1–4)
Social interventions 17.8%	Engaging in hobbies Holding a worthwhile conversation Performing amateur dramatics Having dinner and drinks Attend cinema or theatre	39	2 (range 1–4)
Preservation of normality 13.7%	Going to work Doing household chores Going shopping Writing letters or articles Cooking	54	2 (range 1–2)
Nutritional interventions 6.9%	Adding liver to diet Taking a soothing drink Altering timing of meals	11	2 (range 2–4)
Relief of symptoms and comfort measures 4.1%	Taking medication for chronic conditions Taking anti-emetics Hot bath Calling the doctor	9	2 (range 2–4)

*Effectiveness of self-care actions was recorded on a 4-point scale where 1 = not relieved, 2 = partly relieved, 3 = nearly completely relieved and 4 = completely relieved.

The most common category of *self-care* action was related to the modification or alteration in activity and rest patterns. There were 59.3% of actions in this category and these were used by 83.6% of subjects. All categories of action attained a median effectiveness rating of 2. However, the range of effectiveness ratings differed between categories. No additional categories of *self-care* activities came to light in the final

interview when subjects were asked to reflect on their *self-care* behaviour during the last month.

7.5.1 The relationship of fatigue to performance of self-care

The Mann-Whitney test was used to explore possible associations between the fatigue scores and the performance of *self-care*. The subjects were divided into two groups according to whether they performed *self-care* or not, and the *mean fatigue scores* compared for these two groups. The null hypothesis is that X and Y have the same distribution, i.e. that subjects performing *self-care* would have the same fatigue scores as subjects not performing *self-care*. The alternative hypothesis was proposed, H_1, against which H_0 was tested, that is X is stochastically larger than Y i.e. that the fatigue scores for those performing *self-care* action would be greater than those not performing *self-care* action. The results were as follows:

Mean fatigue score
U=127,367 p = <.01

Extent of fatigue
U=129,821 Not significant

Distress from fatigue
U=135,341 Not significant

Degree to which fatigue interfered with the performance of daily activities/chores
U=125,427 p = <.05

Degree to which fatigue interfered with subjects engaging in activities they enjoyed
U=118.156 p = <.01

With the exception of *distress from fatigue* and *extent of fatigue* there was a significant association between the performance of *self-care* and the recording of higher scores on the fatigue VASs. The lack of a statistical association between the individual VASs concerned with the *extent of fatigue* and *distress from fatigue* is interesting considering the thrust of previous contributions to the literature. This literature (see Rhodes and Watson, 1987, for example) suggested the presence of a theoretical link between symptom distress and self-care activity. The more specific scales concerned with interference with usual life routines, which it could be argued are components of symptom distress, achieved significance.

7.6 Summary

Chapter 7 has been concerned with the results related to the aggregated diary data set. A large percentage of the sample reported fatigue (88.9%) during the time they maintained the diary. On just under half of the diary days completed by subjects, they reported experiencing fatigue to some degree. The late afternoon and late evening periods of the day were perceived by subjects to be the times when they were most likely to be experiencing fatigue Subjects attributed an improved or worsening level of fatigue during this current pulse of chemotherapy to a variety of factors, most notably treatment and the presence or absence of symptoms. A significant relationship was recorded between reports of a change in health which resulted in additional health problems and a higher respondent *mean fatigue score* (U=779, p = <.01).

The respondent *mean fatigue score* for the combined data set was 23.5. The *mean fatigue scores* for the 21-day, 28-day and weekly cycle were 25.9, 18.8 and 23.1 respectively. A Kruskal-Wallis test revealed a significant difference in mean fatigue scores between these three groups. Those patients receiving a 21-day regime were significantly more fatigued than those in the 28-day or weekly group of patients. The RM-ANOVA procedure revealed that the decline in *mean fatigue scores* over time following the administration of chemotherapy was significant in both the 21-day and 28-day cycle, whereas the scores for the weekly cycle remained relatively stable over time and thus failed to attain significance.

When differences in *mean fatigue scores* were examined in relation to the sociodemographic and medical characteristics of the sample significant findings related to the site of cancer (H = 17.4, 7 df, p = <.05), *type of chemotherapy* (H = 20.2, 7 df, p = <.01) and the manner in which the chemotherapy protocol was administered (H = 8.0, 2 df, p = <.01).

The diary contained a record for patients to document *self-care behaviours* and their perceived effectiveness. On the days subjects indicated they were experiencing fatigue *self-care* actions were recorded in response to this problem on approximately half of these days. Subjects were most likely to record a single *self-care* behaviour that was perceived to be partially effective in relieving their fatigue and the most common strategy consisted of taking some sort of rest or a nap during the day. A significant positive relationship was found between the performance of *self-care* and the *mean fatigue score* recorded in the diary U=127,367, p = <.01.

CHAPTER 8

RESULTS III

8.1 Introduction

This chapter details the results derived from analysis of data collected at 7-day intervals using the Holmes Symptom Distress Scale (HSDS), Mood Adjective Checklist (MACL) and the second part of the diary concerned with fatigue. These data were described and examined to detect possible associations between fatigue scores and items on the HSDS and MACL using the Mann-Whitney test. Additionally, associations between demographic, medical variables and scores achieved on these instruments were examined using the Kruskal-Wallis procedure. Data derived from the administration of the Piper Fatigue Scale (PFS) and the Hospital Anxiety and Depression Scale (HADS) at the close of diary completion are also presented. Following this, results of procedures employed to establish validity and internal consistency of the above instruments are presented. In conclusion, a short summary will be offered concerned with the main findings arising from the study.

8.2 Repeated Measurements At Seven Day Intervals

A number of instruments were chosen to facilitate further study of the relationships between fatigue, mood and symptom distress, interspersed at 7-day intervals concurrent with diary keeping. Scores obtained whilst using these instruments, and the results of examining the data for the presence of any associations with fatigue, are reported in section 8.2.

8.2.1 Mood Adjective Checklist

The data were examined in two ways and each was looked at in turn. Firstly, the data were pooled, and secondly examined on a day by day basis. Table 8.1 summarises the median values achieved for the subscales of the MACL when all the recordings were combined (referred to as the pooled data) and when analysed according to the day of completion.

Table 8.1 Median scores achieved on the MACL for pooled data and at seven day intervals

MACL Subscale (score range possible)	Pooled data	Day 7	Day 14	Day 21	Day 28
Tension - Anxiety (0–12)	1	1	1	1	1
Vigour - Activity (0–12)	3	2	3	4	4
Fatigue - Inertia (0–12)	3	4	3	3	2
Anger - Hostility (0–12)	0	0	0	0	0
Depression - Dejection (0–24)	1	2	1	0	0

Data were subdivided into those subjects receiving 21-day, 28-day and weekly cycles of chemotherapy, ranked, and analysed by RM-ANOVA to examine the time effect as a within-subject factor. In the case of those subjects receiving 28-day and weekly cycles of chemotherapy all subscales failed to attain significance, suggesting that there was no significant difference between the observations at the selected time points. For subjects receiving the 21-day cycle the *fatigue - inertia* ($F = 4.75$, $df_1 = 2$ $df_2 27$, $p = <.05$) and *depression - dejection* subscales ($F = 7.44$, $df_1 = 2$ $df_2 = 27$, $p = <.01$) were significant.

Spread of scores was examined by recoding responses in a low, middle or high category as detailed in table 8.2. The percentage of scores obtained in each category for each subscale for the pooled data can be found in table 8.3.

Table 8.2 Categories used and scores assigned when recoding responses to MACL

MACL Subscale	Categories Used And Scores Assigned		
	Low	Middle	High
Tension - Anxiety	0–4	5–8	9–12
Vigour - Activity	0–4	5–8	9–12
Fatigue - Inertia	0–4	5–8	9–12
Anger - Hostility	0–4	5–8	9–12
Depression - Dejection	0–8	9–16	17–24

Table 8.3 Number of observations obtained in the low, middle or high score category on the MACL

MACL Subscale	Low Score	Middle Score	High Score	Total
Tension - Anxiety	258 (88.1%)	31 (10.6%)	4 (1.4%)	293
Vigour - Activity	192 (66.0%)	81 (27.9%)	18 (6.2%)	291
Fatigue - Inertia	181 (61.8%)	88 (30.0%)	24 (8.2%)	293
Anger - Hostility	288 (98.3%)	5 (1.7)	0 (0.0%)	293
Depression - Dejection	268 (91.8%)	22 (7.5%)	2 (0.7%)	292

There were a preponderance of scores in the low category on all subscales of the MACL. Very few respondents achieved a high score on any of the subscales, but when a high score was attained it was more likely to be on the *fatigue-inertia* subscale. There was a complete absence of high scores recorded on the *anger-hostility* subscale.

8.2.1.1 Relationships between subscale scores and mean fatigue score

The Mann-Whitney test was employed to examine possible association between the subscale scores of the MACL and *mean fatigue score* . Subjects were divided into two groups according to low or high scores on the MACL as detailed in table 8.4 and the

Table 8.4 Categories used and scores assigned when recoding responses to MACL

MACL Subscale	Categories Used And Scores Assigned	
	Low	High
Anger - Hostility	0–1	> 1
Depression - Dejection	0–9	10–24
All others	0–5	6–12

mean fatigue scores were compared for these 2 groups. The hypothesis against which H_0 was tested was that a greater subscale score would be associated with a higher *mean fatigue score*, except in the case of the *vigour - activity* subscale where a greater subscale score would be associated with a lower *mean fatigue score*. The results were all significant and were as follows :

Tension - Anxiety	$U = 104$	$p = <.05$
Vigour - Activity	$U = 406$	$p = <.01$
Fatigue - Inertia	$U = 250$	$p = <.01$

Anger - Hostility	$U = 374$	$p = <.01$
Depression - Dejection	$U = 121$	$p = <.05$

The relationship between maximum subscale score and *mean fatigue score* was also examined. In order to find a valid maximum the *depression - dejection* subscale was standardised to bring its theoretical range into line with the other subscales. The maximum score was then coded into 4 groups (0–3 =1, 3–6 = 2, 6–9 = 3 and 9–12 = 4) and the Kruskal - Wallis test applied to compare *mean fatigue scores* across the groups. The result was highly significant (H = 18.72, $3 df, p = <.01$) and examination of the mean ranks and z values revealed that subjects in group 4 i.e. those with the highest maximum score, were clearly different. Because this approach included the subscale scores, and one would logically expect to find a relationship between a maximum value on these subscales and the *mean fatigue score*, a second procedure was undertaken. This procedure omitted the *vigour-activity* and *fatigue-inertia* subscales. The maximum value was derived from each data collection point and data values coded as follows : 0–3 =1, 3–6 = 2 and 6–12 = 3. The results of a Kruskal-Wallis procedure utilising these data and the corresponding *mean fatigue score* proved to be highly significant (H = 39, $2 df, p = <.01$). The mean rank and median value of group 3 were higher than groups 1 and 2.

8.21.2 Relationships between demographic and medical variables and Mood Adjective Checklist subscale scores

To examine relationships between subscale scores on the MACL and selected demographic and medical variables on the MACL, the data were left uncoded, and subjects divided into groups according to the demographic or medical characteristics. Kruskal-Wallis tests were then computed using the "pooled" data. The following sections present the results with the figures in brackets representing the median value and mean rank respectively, as in Chapter 7. Due to the large number of procedures performed which increased the chance of Type I errors occurring (rejecting the null hypothesis when in fact it is true) only those results where $p = <.01$ are reported in this section.

8.2.1.3 Site of cancer

The significant results were as follows when data were examined for significant differences in MACL subscale scores by *site of cancer* :

Tension-anxiety	H = 31.3	7 *df*	$p = <.01$
Vigour-activity	H = 18.0	7 *df*	$p = <.01$
Fatigue-inertia	H = 18.5	7 *df*	$p = <.01$
Depression-dejection	H = 29.5	7 *df*	$p = <.01$

On examining the median and mean rank for *tension-anxiety* (3, 237), *fatigue-inertia* (6, 205) and *depression-dejection* (7, 142) in the different sites it appears that these values are higher in subjects with a diagnosis of pancreatic cancer. *Tension-anxiety* scores were lowest in the breast cancer subjects (0, 108), whereas *fatigue-inertia* scores were lowest in those with an unknown primary (2, 120), and finally *depression-dejection* scores were lowest in those with colorectal (0, 121) and breast cancer (0, 124). In relation to *vigour-activity*, subjects with ovarian cancer achieved the highest values, a median of 4 and mean rank of 165, and lowest in those with pancreatic cancer (0, 80).

8.2.1.4. Previous other treatment

The significant results were as follows when data were examined for significant differences in MACL subscale scores in relation to having received *previous other treatment* for cancer :

Anger-hostility	H = 6.3	1 *df*	$p = <.01$
Depression-dejection	H = 8.2	1 *df*	$p = <.01$

Those subjects who had not received any *other previous treatment* (surgery, radiotherapy and/or endocrine therapy) achieved a higher mean rank in relationship to the *anger-hostility* (0, 156) and *depression-dejection* (2, 159) subscales.

8.21.5. Type of chemotherapy

The significant results were as follows when data were examined for significant differences in MACL subscale scores by *type of chemotherapy* :

Depression-dejection H = 19.7 7 *df* $p = <.01$

On examining the median and mean rank for the *depression-dejection* subscale (3, 171) in those receiving the differing *types of chemotherapy* , it appears that this value is higher in those receiving the ECF protocol and lower in those receiving 5-Fu and Levamisole (0, 105).

8.21.6 Purpose of chemotherapy

The significant results were as follows when data were examined for significant differences in MACL subscale scores by *purpose of chemotherapy* :

Tension-anxiety	H = 12.5	3 *df*	$p = <.01$
Fatigue-inertia	H = 12.3	3 *df*	$p = <.01$
Depression-dejection	H = 12.8	3 *df*	$p = <.01$

On examining the median and mean rank for *tension-anxiety* (1, 163), *fatigue-inertia* (5, 166) and *depression-dejection* (3, 166) by the rationale underlying the chemotherapy, it appears that values are higher in those receiving chemotherapy for locally advanced disease and lowest in those subjects receiving chemotherapy in a neo-adjuvant manner before surgery.

8.2.1.7 Intended outcome

The significant results were as follows when data were examined for significant differences in MACL subscale scores by *intended outcome* of chemotherapy :

Depression-dejection H = 8.0 1 *df* $p = <.01$

On examining the median and mean rank for the *depression-dejection* subscale (2, 157), these values are higher in those receiving chemotherapy for palliative purposes (as opposed to non-palliative).

8.21.8 Nature of administration

The significant results were as follows when data were examined for significant differences in MACL subscale scores by *nature of administration* :

Anger-hostility	H = 10.6	2 *df*	$p = <.01$
Depression-dejection	H = 14.7	2 *df*	$p = <.01$

On examining the median and mean rank for the *depression-dejection* (3, 186) and *anger-hostility* (0, 174) subscales, these values are higher in those receiving chemotherapy by the bolus and continuous route and lowest in those receiving intermittent bolus injections of chemotherapy.

All the remaining subscales, in relation to the above demographic and medical variables, were not significant or failed to achieve significance at $p = <.01$. There were no significant results in relationship to *age*, *gender*, *date of diagnosis*, *disease status*, *pulse number*, *previous chemotherapy*, *presence of liver metastases* and the subscales of the MACL.

8.2.2 Holmes Symptom Distress Scale

These data were examined in a similar way to those obtained with the MACL. Firstly, data were "pooled", then examined on a day by day basis. Table 8.5 shows the scores obtained on the HSDS for the "pooled" data analysed according to the day of completion. Lower scores on the HSDS indicate a greater magnitude of distress for that symptom.

Table 8.5 Mean scores achieved on the HSDS for pooled data and at seven day intervals

Individual items on the HSDS	Pooled data		Day 7		Day 14		Day 21		Day 28	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Pain	83.7	23.3	83.5	23.4	83.7	23.5	83.6	23.7	84.3	23.1
Nausea	86.8	21.4	80.3	25.6	88.6	19.7	89.6	19.8	93.2	11.1
Appetite	79.6	27.1	74.4	27.7	79.1	28.4	82.6	26.8	87.3	20.9
Sleep	71.6	26.5	67.1	26.0	68.2	28.6	78.3	23.9	77.1	25.0
Mobility	78.5	22.0	72.5	22.9	80.4	21.9	81.4	20.0	83.1	21.3
Diarrhoea	84.1	23.3	82.6	23.8	84.6	22.6	85.3	22.7	84.1	25.6
Constipation	82.9	25.6	80.4	26.5	81.4	27.4	84.2	24.7	90.2	20.2
Tiredness	63.7	27.0	56.3	27.0	64.3	29.2	69.1	24.6	69.4	23.2
Concentration	75.8	24.7	69.1	26.4	78.2	22.9	78.7	24.0	81.0	23.2
Mood	68.9	21.6	64.1	20.7	69.3	22.8	72.2	21.4	73.2	19.6
Appearance	65.3	27.4	62.0	26.4	65.6	29.1	67.4	26.8	68.4	27.0
Mean total score	76.4	16.1	72.0	15.3	76.7	16.5	79.3	15.9	81.0	15.1

The mean symptom distress score was 76.4 (SD 16.1) when the items were summed. Scores ranged from 25.9–100. Overall the scores obtained for all items displayed a unimodal distribution: they were positively skewed towards the end of the scale, indicating the absence of a symptom, as had been the case with the diary VASs concerned with symptoms.

As with the MACL, data were subdivided into those subjects receiving 21-day, 28-day and weekly cycles of chemotherapy, ranked, and analysed by RM-ANOVA to examine the time effect as a within-subject factor. In the case of those subjects receiving weekly cycles, all items failed to achieved significance suggesting there was no significant difference between the observations at the selected time points. For subjects receiving a 21-day cycle, *sleep* ($F = 7.27$, $df_1 = 2$ $df_2 = 27$, $p = <.01$), *nausea* ($F = 4.57$,

$df_1 = 2$ $df_2 = 27$, $p = <.05$) and the *total mean score* (F = 5.35, $df_1 = 2$ $df_2 = 30$, $p = <.01$) were significant. The items of *tiredness* (F = 3.77, $df_1 = 3$ $df_2 = 19$, $p = <.05$), *sleep* (F = 4.06, $df_1 = 3$ $df_2 = 19$, $p = .<.05$), *nausea* (F = 5.15, $df_1 = 3$ $df_2 = 19$, $p = .<.01$ and the *total mean score* (F = 4.5, $df_1 = 3$ $df_2 = 22$, $p = <.01$) achieved significance in those receiving a 28-day cycle.

8.2.2.1 Symptoms causing most concern

Further study of the questionnaires permitted identification of those symptoms causing most concern to the subjects. Holmes (1989) proposed this could be achieved by defining significant distress by the arbitrary cut-off point of 50mm (i.e. half the possible total score). These findings are summarised in table 8.6. The symptom of *tiredness* and feelings that *appearance* had deteriorated were reported to be the cause of significant distress in over 40% of the questionnaires completed.

Table 8.6 Percentage of questionnaires reporting significant distress from specific symptoms (score < 50mm on individual items)

Symptom	%
Tiredness	48.9
Appearance	44.9
Mood	35.7
Concentration	25.8
Sleep	24.7
Mobility	21.4
Appetite	20.6
Constipation	20.4
Pain	16.3
Diarrhoea	11.3
Nausea	10.2

Using the same coding criteria as above, in 36.5% of the questionnaires none of the symptoms resulted in severe distress whereas in 20.6% of questionnaires subjects only experienced one symptom causing significant distress, 13.6% experienced 2 symptoms and 29.2% experienced 3 or more.

In answer to the open ended question "Is there any one symptom which is causing you severe distress ?" subjects reported one or more symptoms on 132 (43.9%) out of 301 possible occasions. On 74 (24.6%) occasions subjects reported that there were none.

On the remaining occasions the question was left blank. The most frequently reported symptoms in descending order were : *pain* (32), *hair loss* (29), *nausea* (10), weakness/lack of strength/stamina (8), *diarrhoea* (8), shortness of breath (7), *tiredness* (7) and *appearance* (6). Subjects sometimes qualified their answer by stating that they did not consider the symptom to be producing severe distress, but it was of some concern to them. Subjects opinions of whether their symptoms were caused by "the disease or the treatment" were sought, revealing that on 144 occasions (47.8%) they attributed their symptoms to the treatment. The remainder considered their symptoms to be due to both (38 or 12.6%), to the disease (23 or 7.7%), neither (19 or 6.3%) or they didnt know or were not sure (9 or 3.0%). On 68 (22.6%) occasions subjects did not complete this question.

8.2.2.2 Relationships between Holmes Symptom Distress Scale item scores and mean fatigue score

The Mann-Whitney test was used to examine association between item scores on the HSDS and *mean fatigue score*. The subjects were divided into 2 groups according to low or high scores on the HSDS items, and the *mean fatigue scores* were compared for these 2 groups. H_0 was tested against the hypothesis that a score < 50mm would be associated with a higher *mean fatigue score*. The significant results where p <.05 were as follows :

Pain	$U = 459$	$p =<.05$
Appetite	$U = 414$	$p =<.01$
Mobility	$U = 415$	$p =<.01$
Constipation	$U = 522$	$p =<.05$
Tiredness	$U = 523$	$p =<.01$
Concentration	$U = 404$	$p =<.01$
Mood	$U = 407$	$p =<.01$
Appearance	$U = 667$	$p =<.01$
Total mean score	$U = 248$	$p =<.01$

The remaining items : *nausea, sleep* and *diarrhoea* were not significant. A further procedure was performed where the *tiredness* item was removed as an item contributing to the total mean score. A significant result was still achieved following this manipulation ($U = 303$, $p =<.01$).

These data were examined further through the selection of maximum values achieved at each data collection point. As above, subjects were divided into 2 groups

according to low or high scores on the HSDS items and the *mean fatigue scores* compared for these 2 groups. H_0 was tested against the hypothesis that a score < 50mm would be associated with a higher *mean fatigue score*.. The result was highly significant ($U = 5,536$, $p = <.01$).

8.2.2.3 Relationships between demographic and medical variables and Holmes Symptom Distress Scale item scores

To examine relationships between item scores on the HSDS and selected demographic and medical variables, subjects were divided into groups according to the demographic or medical characteristic. Kruskal-Wallis test statistics were then computed using the "pooled" data. As with the analysis relating to the MACL data there was the likelihood of Type I errors because of the large number of procedures performed (rejecting the null hypothesis when in fact it is true). Thus only those results where $p = <.01$ are reported in this section.

8.2.2.4 Gender

The significant results were as follows when data were examined for significant differences in item scores by *gender* :

Pain	H = 7.4	1 *df*	$p = <.01$
Sleep	H = 6.5	1 *df*	$p = <.01$

On examining the median and mean rank for *pain* (92, 133) and *sleep* (74, 134) these values were lower in men.

8.2.2.5 Site of cancer

The significant results were as follows when data were examined for significant differences in item scores by *site of cancer* :

Pain	H = 23.8	7 *df*	$p = <.01$
Nausea	H = 25.4	7 *df*	$p = <.01$
Appetite	H = 28.5	7 *df*	$p = <.01$
Sleep	H = 31.4	7 *df*	$p = <.01$

Mobility	H = 35.6	7 *df*	$p = <.01$
Diarrhoea	H = 33.4	7 *df*	$p = <.01$
Concentration	H = 34.5	7 *df*	$p = <.01$
Appearance	H = 22.2	7 *df*	$p = <.01$
Total mean score	H = 23.4	7 *df*	$p = <.01$

On examining the median and mean rank for *pain* (35, 61), *nausea* (54, 64), *appetite* (54, 84), *sleep* (49, 59) and *mobility* (67, 74) values were lower in subjects with an unknown primary. Subjects with a pancreatic or biliary duct cancer attained a lower mean rank and median value for *diarrhoea* (71, 84), *concentration* (52, 70) and *appearance* (48, 105). The *total mean score* was lowest in those with an unknown primary (56, 70) and highest in those with ovarian cancer (83, 176)

8.2.2.6 Type of chemotherapy

The significant results were as follows when data were examined for significant differences in item scores by *type of chemotherapy* received :

Pain	H = 21.3	7 *df*	$p = <.01$
Nausea	H = 27.4	7 *df*	$p = <.01$
Appetite	H = 29.9	7 *df*	$p = <.01$
Sleep	H = 40.4	7 *df*	$p = <.01$
Mobility	H = 31.7	7 *df*	$p = <.01$
Diarrhoea	H = 27.1	7 *df*	$p = <.01$
Concentration	H = 24.7	7 *df*	$p = <.01$
Appearance	H = 18.5	7 *df*	$p = <.01$

On examining the median and mean rank for *pain* (62, 70), *nausea* (79, 66), *appetite* (79, 93), *sleep* (53, 69), *mobility* (75, 77) and *concentration* (68, 72) values were lower in subjects receiving Cisplatin and 5-Fu.

Subjects receiving 5-Fu and Levamisole attained a lower mean rank and median value for *diarrhoea* (68, 72), whereas subjects receiving Etoposide and Epirubicin achieved a lower mean rank and median value for *appearance* (50, 101).

Higher scores reflecting lower levels of symptom distress were recorded in those receiving CMF for the *pain* (100, 188) *nausea* (100, 190), *appetite* (99, 168), *mobility* (99, 203), *diarrhoea* (100, 192) and *concentration* (98, 188) items. Subjects receiving

weekly 5-Fu injections recorded higher scores for the *sleep* (96, 183) and *appearance* VASs (88, 169).

8.2.2.7 Nature of administration

The significant results were as follows when data were examined for any significant differences in item scores according to the method used to administer chemotherapy :

Appetite	H = 10.6	2 *df*	$p = <.01$
Diarrhoea	H = 15.8	2 *df*	$p = <.01$
Appearance	H = 8.7	2 *df*	$p = <.01$

On examining, the median and mean rank for the *appetite* (81, 118) and *appearance* (51, 130) items, these values were lowest in subjects receiving bolus and continuous chemotherapy and higher in those receiving bolus and/or short term infusions (94, 162) and intermittent bolus injections (80, 177) respectively. Subjects receiving chemotherapy by the intermittent bolus route achieved a lower mean rank and median value for *diarrhoea* (90, 117) compared to subjects receiving chemotherapy by bolus and/or short term infusion (97, 163).

7.2.2.8 Pulse

The significant results were as follows when data were examined for significant differences in item scores by *pulse* number :

Pain	H = 19.9	5 *df*	$p = <.01$
Nausea	H = 17.7	5 *df*	$p = <.01$
Appetite	H = 17.5	5 *df*	$p = <.01$
Mobility	H = 23.7	5 *df*	$p = <.01$
Diarrhoea	H = 24.3	5 *df*	$p = <.01$
Total mean score	H = 15.2	5 *df*	$p = <.01$

On examining, the median and mean rank for *pain* (83, 76), *nausea* (91, 90), *appetite* (82, 88), *mobility* (71, 79) and *diarrhoea* (90, 84) values were lower in subjects receiving their first pulse of chemotherapy. The *total mean score* was lowest during the first pulse (74, 94) and highest during the fifth pulse (86, 139).

8.2.2.9 Previous other treatment

The significant results were as follows when data were examined for significant differences in item scores according to whether subjects had received any other *previous treatment*:

Appearance	H = 7.9	1 *df*	$p = <.01$
Mobility	H = 6.3	1 *df*	$p = <.01$

On examining the median and mean rank for *appearance* (62, 136) and *mobility* (80, 138) values were lower in those subjects who had not received any other treatment prior to this chemotherapy

All the remaining items on the HSDS and the *total mean score* in relationship to the above demographic and medical variables failed to achieve significance. In addition scores achieved on the HSDS and the following variables were not significant at $p=<.01$: *age, date of diagnosis, disease status, intended outcome, purpose of chemotherapy, previous chemotherapy* and the *presence of liver metastases.*

8.3 Piper Fatigue Scale

As reported in Chapter 6, subjects who had completed the diary keeping task were offered the chance to complete the PFS to further assess this instrument following the problems encountered in the pilot phase (see Chapter 5). The first 21 subjects were approached to complete this instrument, but of these only 2 managed to complete all of the items on the questionnaire. These data were incomplete and only the mean score for each dimension is reported (see table 8.7). Where necessary mean item substitution was employed. This was not attempted when less than 75% of items for a dimension had not been completed. After the recruitment of subject 21, it was not felt beneficial to the study to ask any further subjects to complete this instrument.

Table 8.7 Data derived from the completion of the PFS by 21 subjects

PFS dimension (no. of items included in dimension)	Number of subjects completing dimension	% of questions answered within each subscale and whole questionnaire	Mean score	SD
Temporal (4)	10	61.9	47.2	22.1
Intensity (12)	14	72.2	34.2	25.6
Affective (5)	4	21.0	59.2	13.7
Sensory (15)	18	82.5	46.4	18.6
Total Mean Fatigue Score	4	69.6	59.1	10.3

Further analysis of the questionnaires revealed the most commonly omitted questions in each dimensions. These were as follows: within the *temporal* dimension questions 4 and 5; within the *intensity* dimension questions 8 and 18; within the *affective* dimension, questions 21 and 22; and within the *sensory* dimension no question appeared more poorly completed than any other.

Responses to the open questions were tallied. Subjects had most often been feeling fatigued for weeks (4/11 subjects) rather than minutes, hours, days or months The most common reply to question 42 concerned with what the respondent believed to be most directly contributing to or causing their fatigue was chemotherapy (5/11 subjects) and the best relief measure (question 43) involved taking a rest (4/7 subjects). The majority of subjects did not report experience of symptoms at the time of completion (13/15 subjects).

8.4 Hospital Anxiety And Depression Scale

As reported in Chapter 5 suspension of the PFS from data collection resulted in the opportunity to incorporate a further instrument into data collection - and after consideration it was decided to include the HADS. Thirty-eight subjects completed this questionnaire. The two subscales, one measuring anxiety (*A-scale*) and one measuring depression (*D-scale*) are scored separately. Scoring bands developed by (Snaith and Zigmond, 1994). were used in this analysis. The bands are: 0–7 = normal, 8–10 = mild, 11–14 = moderate and 15–21 = severe Table 8.8 summarises the percentage of subjects occupying each scoring band for the *A-scale* and *D-scale*. The majority of subjects occupied the *normal* band, and there were no subjects in the *severe* band in this sample. The median scores for the *D-scale* and *A-scale* were 4 (range 0–12) and 4 (0–12) respectively.

Table 8.8 Number of subjects in each category according to HADS subscale scores

Scale Scores	Number of cases in A - scale	Number of cases in D- scale
Normal (0–7)	29 (76.3%)	29 (76.3%)
Mild (8–10)	5 (13.2%)	7 (18.4%)
Moderate (11–14)	4 (10.5%)	2 (5.3%)
Severe (15–21)	0	0

8.4.1 Relationships between Hospital Anxiety and Depression Scale scores and mean fatigue score

The Mann-Whitney procedure was utilised to examine for possible association between the HADS scores and *mean fatigue score*. The subjects were divided into 2 groups instead of four (due to small sample sizes in some categories) according to normal or above normal scores on the HADS, and the *mean fatigue scores* compared for these 2 groups. H_0 was tested against the hypothesis that a lower subscale score would be associated with a lower *mean fatigue score*. The results were significant and were as follows:

A-scale	$U = 55$	$p = <.01$
D-scale	$U = 42$	$p = <.01$

8.4.2 Relationships between demographic and medical variables and Hospital Anxiety and Depression Scale scores

To examine relationships between HADS scores and selected demographic and medical variables, data were left uncoded, and subjects divided into groups according to the demographic or medical feature. Kruskal-Wallis test statistics were then computed. However, no significant differences were revealed.

8.5 General Linear Models

As a number of relationships between fatigue and the demographic variables had been suggested during the preceding analysis, computation of general linear models (GLM) were attempted using the relevant Minitab command. This procedure allows the calculation of multiple ANOVA tables and the examination of interactive effects between variables entered into the model upon the response - fatigue, where the nature of the data yields an unbalanced design. Data were ranked before the computation to avoid violation of some of the assumptions and requirements upon which ANOVA is based and which the GLM procedure could not handle. However, the computation of models was impossible in many cases because insufficient data were present in some of the categories due to the empty cells or incomplete "nesting". Even when computation was possible, it failed to produce any further useful information than that obtained utilising the Kruskal-Wallis non-parametric one-way analysis of variance procedures already reported.

8.6 Section Summary

The HSDS and MACL were completed at 7-day intervals alongside the task of diary completion to facilitate the study of the relationships between fatigue, mood and symptom distress. Scores obtained with these instruments and results yielded by examination of the data for association with fatigue, sociodemographic and medical variables have been outlined in the preceding sections.

In summary, scores recorded on both the MACL and HSDS indicated a lack of mood disturbance and low levels of symptom distress. In the case of the MACL, greater subscale scores were associated with higher *mean fatigue scores*, except in the case of the *vigour-activity* subscale where a greater *mean fatigue score* was associated with a lower subscale score. Similarly a significant result was recorded when the association between *mean fatigue scores* and symptom distress was examined: higher levels of symptom distress were associated with greater *mean fatigue scores*. *Tiredness* and negative feelings about *appearance* were responsible for causing a significant degree of distress in over 40% of scales completed.

When differences in symptom distress scores and MACL subscale scores were examined in relation to the sociodemographic and medical characteristics of the sample a number of significant findings emerged. For example, the total *mean symptom distress score* was lowest during the first *pulse* (indicating a greater level of symptom distress) and highest during the fifth *pulse* of chemotherapy. Scores achieved on the HSDS and the following variables were not significant: *age*, *date of diagnosis*, *disease status*, *intended outcome*, *purpose of chemotherapy*, and the *presence of liver metastases*. In the case of the MACL there were no significant results in relationship to *age*, *gender*, *date of diagnosis*, *previous chemotherapy*, *presence of liver metastases* and the MACL subscales. There were, however, a number of significant findings. For example, when MACL subscale scores were examined for significant differences by *intended outcome* of chemotherapy, subjects receiving chemotherapy for palliative as opposed to non-palliative purposes attained a higher median score in relation to the *depression-dejection* subscale.

8.7 Internal Consistency And Validity Of Data Collection Tools

The final aim of the study was concerned with testing aspects of reliability and validity of the instruments used in the description of fatigue and the other variables, namely the VASs in the diary, the HSDS, MACL and HADS. Estimates of the reliability of the HSDS, MACL, HADS and 4 VASs concerned with fatigue were obtained through assessment of internal consistency using the method described by Cronbach (1951). This is based on an estimate of the proportion of variance due to all the common factors present among the items. It provides an indication of the extent to which an instrument coheres i.e. how successfully it is measuring the same type of concepts. According to Carmines and Zeller (1979) the coefficient should not fall below .80.

Validity is the extent to which any instrument measures what it intended to measure. Validation is not of the instrument itself, but of the purpose for which it is currently being employed. The concepts described by Campbell and Fiske's (1959) of convergent and discriminant validity, can be seen as a logical extension of construct validity in which each of the constructs is measured by multiple methods. Convergent validity refers to the extent to which different methods of measuring the same trait yield similar results. The fundamental assumptions are that different methods of measuring the same trait should converge on the same result. Discriminant validity refers to the extent to which similar or identical methods of measuring different traits lead to different results. Thus discriminant validity implies that traits that are truly distinct from one another should lead to different results even if they are measured by the same method. Convergent and discriminant validity of the HSDS, MACL and fatigue diary items were examined with reference to the combined correlation matrix of the MACL, HSDS and items in the daily diary.

Factor analysis is a statistical technique which can be used to assess the reliability and validity of empirical measurements. Essentially factor analysis consists of a variety of statistical methods leading to the representation of a set of variables in terms of a smaller number of hypothetical factors. Each factor is defined by those items correlating more highly with each other than with the other items. Factor loading gives a statistical indication of the extent to which an item is correlated with a factor. The higher the factor loading, the more the particular item contributes to that factor. Each factor is a combination of items. The factors are usually rotated so that the items defining a factor are correlated most strongly with each other rather than the remaining items.

For the current analyses exploratory factor analyses were performed with the HSDS, MACL and HADS to identify the components contained within each instrument using the SPSS - Release 4 statistical package. The results will be compared to previous analyses in Chapter 9. Data for these analyses were derived from the repeated administration of these instruments on day 7, 14 and 21 (and day 28 when relevant), or single administration in the case of the HADS. The basis of both analyses is a correlation matrix built up from the relevant variables. The principal components method was adopted to obtain the initial solutions. Here a component is calculated to explain the maximum variance in all the variables, then a second component is calculated to explain the maximum amount of the remaining variance, although it cannot be correlated with the first component.

Scree plots were used as an aid to identifying the number of components to usefully retain in each instrument. These plot the eigenvalues in descending order. Cattell (1965) advocates the cessation of factoring at the point where the eigenvalues begin to level off, forming a straight line. Eigenvalue statistics of >1 were selected as the values that would be used as the cut off point. This is the most commonly used procedure for determining the number of initial factors to be extracted (Kim and Mueller, 1978). There are an infinite number of alternative solutions and this leads to component rotation, the second stage in the analysis. The provisional components are transformed in order to find new components that are easier to interpret. Rotation is possible using a number of approaches, in order to find a solution open to interpretation. Orthogonal and oblique rotations were used in the present analysis. Varimax, a method of orthogonal factor rotation, simplifies the columns of the component loading matrix by maximising the variance of the squared loadings. Its advantage is that the calculation is performed to maximise the tendency of each variable to load highly on only one component (Manley, 1986). It results in a unique rotated component loading matrix and is recommended as the standard approach. The oblique method of rotation does not make the assumption of the orthogonal type rotation, which is that the underlying components are uncorrelated, thus allowing for the possibility that the components might show correlation with each other.

8.7.1 Holmes Symptom Distress Scale

Study of the correlation matrix in figure 8.1 revealed that the majority of items attained statistically significant correlations (r_s) of .26 or greater, a high level of significance in a large sample such as this (p=.01). This result suggests that for the HSDS most symptoms are closely interrelated.

Figure 8.1 Spearman's correlation coefficient matrix obtained for HSDS in 292 cases

2	.53									
3	.60	.65								
4	.32	.36	.35							
5	.62	.45	.63	.33						
6	.28	.40	.43	.31	.26					
7	.53	.48	.49	.33	.39	.26				
8	.31	.31	.49	.43	.41	.29	.34			
9	.49	.47	.61	.42	.67	.27	.43	.61		
10	.36	.36	.52	.42	.51	**.23**	.32	.64	.71	
11	.27	.20	.35	.33	.38	**.23**	**.22**	.42	.51	.53
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**

N.B. **Bolded** = significant at 5% level ($p < .05$). Remainder significant at $p < .01$

1 = Pain. 2 = Nausea. 3 = Appetite. 4 = Sleep 5 = Mobility. 6 = Diarrhoea. 7 = Constipation. 8 = Tiredness. 9 = Concentration. 10 = Mood. 11 = Appearance.

Internal consistency was high in HSDS resulting in a Cronbach's α of .86.

Factor analysis was performed with 292 sets of scores. Extraction resulted in 2 components with eigenvalues >1. The extraction of these components resulted in 55.1% of the variance being explained within this sample. The first component held an eigenvalue of 4.87 with 44.3% of the variance explained, whereas component 2 held an eigenvalue of 1.19 with 10.8% of the variance explained. However, this solution only accounted for 55.1% of the total variance, leaving 44.9% unexplained. Holmes (1989), in her original analysis of this scale, presented the first five principal components extracted accounting for 78.9% of the variance, although only the first component achieved an eigenvalue of >1. This first component included all the items, except *diarrhoea*, accounting for 46.4% of the variance. However, items only achieved loadings of .3. In the light of this, it was decided in addition to the above procedure to force extraction using 5 components to compare the results with the previous analysis. Using this approach 77.2% of the variance was explained.

A varimax (orthogonal) rotation was then performed to obtain more straightforward and readily interpretable results. Table 8.9 reveals the results of the factor analysis following rotation for data derived from the HSDS with a 2 component solution.

Table 8.9 Components derived utilising a principal components approach to factor analysis with data derived from HSDS

Item on the Holmes Symptom Distress Scale	Component 1	Component 2	
Pain	.76		
Mobility	.75		
Appetite	.74		
Nausea	.72		
Constipation	.67		
Mood		.76	
Tiredness		.74	
Appearance		.66	
Concentration		.64	
Diarrhoea		.55	
Sleep		.53	
% of Variance accounted for	44.3	10.8	**Total** 55.1

N.B. Only the main contributors of each component are shown

Component 1 appears to contain items which arguably could be related to the physical dimension of symptom distress, whereas component 2 contains items with a psychological bias, except for *diarrhoea.* Although two dimensions are evident there is still considerable variability unexplained and there does not appear to be a satisfactory reduction in dimensions achieved with this solution.

The rotated factor matrix with a 5 component extraction is presented in table 8.10. Using this approach the first component contains items which could be argued to fall within the psychological domain of symptom distress. *Pain* and *mobility* comprising component 2 and *nausea, appetite* and *constipation* comprising component 3 could be supported on clinical grounds. The fourth and fifth component comprise only a single item each.

Table 8.10 Components derived utilising a principal components approach to factor analysis with data derived from HSDS - 5 factors forced

Item	Component 1	Component 2	Component 3	Component 4	Component 5	
Mood	.81					
Appearance	.77					
Concentration	.72					
Tiredness	.71					
Pain		.88				
Mobility		.75				
Nausea			.91			
Appetite			.54			
Constipation			.43			
Sleep				.87		
Diarrhoea					.91	
% of Variance accounted for	44.3	10.8	8.4	7.5	6.2	77.2

N.B. Only the main contributors of each component are shown

8.7.2 Mood Adjective Checklist

The strength of the relationship of all of the MACL subscales was significant, except for the *anger - hostility* subscale with *vigour - activity*. *Vigour - activity* items as expected, were inversely correlated (see figure 8.2).

Figure 8.2 Spearman's correlation coefficient matrix obtained for MACL in 285 cases

Vigour-Activity	–.43			
Fatigue-Inertia	.58	–.60		
Anger-Hostility	.49	**–.19**	.35	
Depression-Dejection	.62	–.50	.67	.55
	Tension-Anxiety	**Vigour-Activity**	**Fatigue-Inertia**	**Anger-Hostility**

N.B. **Bolded** = not significant at 5% level ($p < .05$). Remainder significant at 1% level ($p < .01$).

Several methods were used to estimate internal consistency of the MACL. Firstly, each individual item comprising the 24 item scale was used to compute a reliability coefficient. This approach yielded an α of .81. The result of inverting the

vigour-activity items increased the estimate to an α of .93. Secondly, the subscales were examined through estimating the α of each individual subscale. The results of this approach were as follows: the *tension-anxiety* subscale yielded an α of .83, the *vigour-activity* subscale yielded an α of .89, the *fatigue-inertia* subscale yielded an α .91, the *anger-hostility* subscale yielded an α of .66 and the *depression-dejection* subscale yielded an α of .89. Individual subscale values would be anticipated to be equal to or higher than the value obtained in the first calculation as items constituting a subscale should cohere more strongly since they are measuring the same concept using slightly different words. Each subscale excepting the *anger-hostility* subscale appeared to be consistently measuring different aspects of mood.

Finally, the result of combining the five subscales (with items constituting the *vigour-activity* scale inverted) was considered, providing an indication of how the subscales formed the total scale. This yielded a standardised α of .86. Using this approach the effect of the lower coefficient for the *anger-hostility* subscale could be more clearly seen. Often when subscales are brought together they fail to result in a high correlation but the overall performance of the combined scale remains within acceptable limits, as in this case. It is often useful if subscales measure different but related concepts. The MACL appeared to be measuring five relatively independent concepts successfully and at the same time the overall performance of the scale in estimating mood disturbance (when *vigour-activity* items are inverted) was also acceptable within this sample.

Factor analysis was carried out on 285 sets of scores. Extraction resulted in 5 components all with eigenvalues > 1. The extraction of 5 components results in 67.2 of the variance being explained within this sample (see table 8.11).

Table 8.11 Extraction analysis for the MACL using the principal components method

Component	Eigenvalue	% of variance	Cumulative %
1	9.36	39.0	39.0
2	2.90	12.1	51.1
3	1.48	6.2	57.3
4	1.27	5.3	62.6
5	1.11	4.6	67.2

Table 8.12 Components derived utilising a principal components approach to factor analysis with data derived from MACL

Adjective	Component 1 Depression-Dejection	Component 2 Tension-Anxiety	Component 3 Fatigue-Inertia	Component 4 Vigour-Activity	Component 5 Anger-Hostility
Hopeless	.80				
Worthless	.69				
Discouraged	.64				
Miserable	.63				
Helpless	.61				
Guilty	.57				
On edge		.83			
Tense		.82			
Nervous		.76			
Unhappy	.51	(.58)			
Depressed	.52	(.54)			
Resentful		(*.51*)			.19
Shaky		.38			
Weary			.87		
Tired			.77		
Worn-out			.75		
Sluggish			.74		
Lively				.83	
Vigorous				.83	
Active				.82	
Full of pep				.80	
Furious					.86
Angry					.81
Spiteful					.44

N.B. Only the main contributors to each component are shown, except when it was expected that an item would load highly but fails to do so, this loading is also included for information. The values in brackets loaded relatively highly on an unpredicted component.

Table 8.12 reveals the results of the factor analysis following rotation by the varimax method for data derived from the MACL. The first principal component, *depression-dejection*, explained 39% of the variance within the data. It achieved high loadings on the relevant items and correspondingly low loadings on the remaining items. This component explained a fair proportion of the variance within this data set. In

contrast the fifth component, *hostility-anger* only accounted for 4.6% of the variance. On the whole, adjectives loaded with their corresponding component suggesting that the components had been appropriately labelled. There were however some notable exceptions. *Shaky*, an adjective grouped within component 2 (*tension-anxiety*) behaved poorly, only achieving a loading of .38. *Resentful*, an adjective associated with the *anger-hostility* subscale only achieved a loading of .19 within its corresponding component, and in fact reached its highest loading within component 2 (.51), the *tension-anxiety* component.

The second component of *tension-anxiety* attracted 2 of the *depression-dejection* variables, *unhappy* (.58) and *depressed* (.54). It appears that these two adjectives contribute significantly to more than one component, the *depression-dejection* and *tension-anxiety* component.

8.7.3 Diary

The internal consistency of each of the 4 VASs concerned with fatigue was computed resulting in a Cronbach's α of .91. As previously reported in Chapter 6, correlation coefficients amongst the individual fatigue VASs were all above .9.

The combined correlation matrix utilised to assess convergent and discriminant validity of the MACL, HSDS and fatigue items of the daily diary can be found in figure 8.3. The majority of correlations were significant : out of a matrix of 208 coefficients, only 26 proved not be significant.

The strongest significant correlations were between the four fatigue items in the daily diary. Strong correlations were also obtained between : *fatigue* items in the daily diary and the *tiredness* item on the HSDS (ranging from –.49 to –.53), the *fatigue-inertia* subscale of the MACL (ranging from .59 to .62) and the *fatigue* items in the daily diary, and the *fatigue- inertia* subscale and the *tiredness* item of the HSDS (–.76). Interestingly, the *concentration* , *mood, mobility* and *appearance* items on the HSDS were significantly correlated with all the MACL subscales and the *fatigue* items in the daily diary. The *sleep* item on the HSDS correlated significantly with all items concerned with *fatigue* in the daily diary except the *distress* item, and in addition with the *depression-dejection* and *fatigue-inertia* subscales.

Consistently non-significant correlations at the 1% level were found between the *diarrhoea* and *constipation* items on the HSDS and *fatigue* items in the daily diary and

Figure 8.3 Correlation matrix derived from items on the HSDS, MACL and the daily diary

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
2	.53																				
3	.60	.65																			
4	.32	.36	.25																		
5	.62	.45	.63	.33																	
6	.28	.40	.43	.31	.26																
7	.53	.48	.50	.33	.40	.26															
8	.31	.31	.49	.43	.41	.30	.31														
9	.50	.47	.61	.42	.67	.27	.43	.61													
10	.36	.35	.52	.42	.51	.23	.32	.64	.71												
11	.27	.20	.35	.33	.39	.23	.22	.42	.51	.53											
12	−.16	−.29	−.34	−.25	−.40	−.26	−.27	−.44	−.54	−.50	−.35										
13	.13	.13	.37	.19	.35	.18	.10	.56	.45	.59	.40	−.42									
14	−.26	−.26	−.41	−.34	−.50	−.25	−.21	−.76	−.61	−.62	−.45	.58	−.60								
15	.09	−.20	−.24	−.17	−.32	−.08	−.14	−.25	−.36	−.40	−.33	.49	−.19	.35							
16	−.30	−.27	−.43	−.27	−.44	−.16	−.28	−.53	−.61	−.68	−.51	.62	−.50	.67	.55						
17	−.27	−.16	−.34	−.27	−.35	−.14	−.12	−.53	−.45	−.51	−.36	.34	−.43	.62	.20	.44					
18	−.29	−.20	−.36	−.28	−.35	−.09	−.13	−.49	−.48	−.51	−.36	.37	−.41	.58	.20	.45	.94				
19	−.30	−.18	−.38	−.24	−.39	−.12	−.15	−.52	−.50	−.54	−.40	.38	−.47	.62	.20	.49	.95	.95			
20	−.32	−.19	−.38	−.26	−.40	−.11	−.15	−.50	−.49	−.53	−.40	.38	−.45	.60	.20	.48	.94	.95	.98		
21	−.30	−.19	−.37	−.27	−.38	−.11	−.15	−.53	−.49	−.54	−.39	.39	−.46	.62	.21	.48	.98	.97	.99	.98	
22	.59	.55	.75	.58	.72	.44	.52	.74	.82	.79	.65	−.56	.54	−.69	−.36	−.53	−.52	−.55	−.55	−.55	−.55

KEY : *Bolded = significant at the 1% level ($p < .01$).*

1 = Pain. 2 = Nausea. 3 = Appetite. 4 = Sleep. 5 = Mobility. 6 = Diarrhoea. 7 = Constipation. 8 = Tiredness. 9 = Concentration. 10 = Mood. 11 = Appearance. 22 = Total mean score

All the above are items on the Holmes Symptom Distress Scale or scores derived from these items

12 = Tension - Anxiety. 13 = Vigour - Activity. 14 = Fatigue - Inertia. 15 = Anger - Hostility. 16 = Depression - Dejection.

All the above are subscales of the Mood Adjective Checklist

17 = Extent of fatigue. 18 = Distress from fatigue. 19 = Interference with ability to carry out daily activities. 20 = Prevented from doing things that are enjoyed. 21 = Mean fatigue score.

All the above are fatigue items in the daily diary or scores derived from these items.

the subscales of the MACL, except *tension-anxiety* with *diarrhoea* (–.26) and *fatigue-inertia* with *diarrhoea* (–.25) and *depression-dejection* with *constipation* (–.27) and *diarrhoea* (–.26).

8.7.4 Hospital Anxiety And Depression Scale

Correlation matrices for the *A-scale* and *D-scale* were computed and are displayed in figure 8.4 and 8.5. The majority of the coefficients are significant in both scales although in the *A-scale* the correlation between the items "I get a sort of frightened feeling like butterflies in my stomach" (item 9) and "I feel restless as if I have to be on the move" (item 11) and in the *D-scale* "I have lost interest in my appearance"(item 10) and "I feel as if I am slowed down "(item 8) failed to achieve significance.

Figure 8.4 Spearman's correlation coefficient matrix obtained for the *A-scale* in 38 subjects

3	.68					
5	.56	.57				
7	.47	.48	.49			
9	.33*	.48	.60	.32*		
11	.33*	.50	.37*	.39*	.31	
13	.49	.50	.49	.63	.56	.45
	1	3	5	7	9	11

N.B. Numbers correspond to items on the HADS scale representing anxiety

* denotes values significant at $p = .05$. Bolded value denotes a non-significant coefficient.

The remaining values are significant at $p = .01$

Figure 8.5 Spearman's correlation coefficient matrix obtained for the *D-scale* in 38 subjects

4	.67					
6	.42	.68				
8	.49	.41	.44			
10	.40	.38*	.33*	.24		
12	.67	.66	.45	.61	.48	
14	.68	.62	.38*	.45	.36*	.62
	2	4	6	8	10	12

N.B. Numbers correspond to items on the HADS scale representing depression

* denotes values significant at $p = .05$. Bolded value denotes a non-significant value.

The remaining values are significant at $p = .01$

Cronbach's α for the *A-scale* was .84 and for the *D-scale* was .82. Scores achieved using the HADS were correlated with the relevant subscale of the MACL in the subsample of subjects who completed the HADS (26 sets of observations were available for this analysis). A modest Spearman's correlation coefficient of .35 (p =<.05) was achieved between the *A-scale* and the *tension-anxiety* subscale and of .43 (p =<.05) between the *D-scale* and the *depression-dejection* subscale.

Factor analysis was carried out on 38 sets of HADS scores. Surprisingly, 4 rather then 2 components emerged. This accounted for 72.8% of the variance (see table 8.13). The eigenvalue of the first component was considerable and accounted for 46.4% of the variance, indicating that an argument could be made for a single component solution.

Table 8.13 Extraction analysis for the HADS using the principal components method

Component	Eigenvalue	% of variance	Cumulative %
1	6.5	46.4	46.4
2	1.6	11.3	57.7
3	1.1	7.9	65.6
4	1.0	7.2	72.8

An orthogonal rotation was performed; using the criterion of loading of .45 as a cut-off point as in earlier analysis (Moorey, Greer, Watson *et al.*, 1991). The anxiety and depression factors were scattered throughout the four components without any clear indication of any separation of the factors. A similar pattern resulted when a 2 component solution was forced.

An oblique rotation was then performed utilising the forced 2 component solution. Moorey *et al.* (1991) considers that oblique rotation could provide a more psychologically meaningful way of analysing data from this instrument. As stated earlier this method of rotation does not make the assumption of the orthogonal rotation: the underlying factors are not correlated, thus allowing for the possibility that the factors might show correlation with each other. There is considerable debate over whether anxiety and depression exist as separate entities (Stavrakaki and Vargo, 1986). Moreover, subscales of anxiety and depression frequently show high correlations. As above, in the case of the orthogonal rotation, it was not possible to reproduce the results of the previous factor analysis by Moorey, Greer, Watson *et al.* (1991). There was a correlation of –.50 between the 2 components when an oblique rotation was performed.

8.8 Summary Of Main Findings

The preceding three chapters have provided a description of the results derived from this study. As outlined in Chapter 5 there were four key aims that the researcher wished to meet in order to fulfil the purpose of the study. These were to:

(A) Monitor the subjective dimensions of fatigue (including information concerned with the onset, pattern, duration, intensity and distress caused by this phenomenon), as documented by the subjects in a daily diary designed by the researcher, and maintained over the period of 21-28 days following the administration of a pulse of chemotherapy.

(B) Describe the nature of the relationship between factors associated with fatigue in this patient population which may influence it, such as mood as measured by the Mood Adjective Checklist (Lishman, 1972), symptom distress as measured by the Holmes Symptom Distress Scale (Holmes, 1989), and a selection of demographic variables associated with this population such as the type, pattern and nature of chemotherapy drugs received, stage of disease and type of cancer.

(C) Describe the self-care interventions which patients utilise in response to fatigue and the perceived effectiveness and source of ideas for such interventions.

(D) Test aspects of reliability and validity of the instruments used in the description of fatigue and the other variables, namely the Holmes Symptom Distress Scale, Mood Adjective Checklist, Fatigue Diary and the Piper Fatigue Scale.

A number of substantive findings emerged in relation to these four areas. The onset, pattern and duration of fatigue appear to be associated with the pattern of drug administration. Distinct patterns emerged in relation to both type of chemotherapy and nature of administration. The *intensity* of fatigue and *distress* resulting from it were very varied, at times severe but at other times absent or relatively mild. The selection of a variety of different approaches to data analysis, such as time series analysis, which is infrequently used in nursing research, facilitated a detailed observation of the phenomenon of fatigue.

More traditional methods of statistical analysis revealed the demographic and medical characteristics which were associated with increased fatigue scores. The *intensity* of fatigue and the other dimensions of this phenomenon selected for measurement in this study were related to both the *site of cancer* and *type of*

chemotherapy subjects received. It is not possible to say if the patterns are independent of *site of cancer*.

Both aspects of *mood* and *symptom distress* were moderately to strongly correlated with the dimensions of fatigue, although overall levels of mood disturbance and symptom distress were not high in this sample. Thus, it could be suggested that fatigue in this sample was an independent factor, not a component, of affective disturbance.

A number of interesting findings resulted from the analysis of the *self-care* data. On half of the days that subjects reported fatigue they undertook some form of *self-care* behaviour. Subjects performed a variety of different *self-care* behaviours in response to fatigue, and these were most frequently concerned with modifying or altering activity and rest patterns, utilising psychological strategies or seeking to preserve some sense of normality in their lives through engaging in everyday activities such as doing the household chores and continuing with paid employment. The *self-care* behaviours selected by this sample had a median effectiveness rating of 2 (on a scale of 1 to 4). Overall there was a significant positive association between the performance of *self-care* and *mean fatigue scores*.

Finally, the results from procedures concerned with estimating various aspects of reliability and validity of the data collection instruments were described. A variety of factor analyses, estimates of internal consistency and correlation matrices were developed and suggest that on the whole the instruments selected achieved satisfactory levels of reliability and validity with this sample.

CHAPTER 9

DISCUSSION AND INTERPRETATION OF RESULTS

9.1 Introduction

This chapter considers the study findings, offering a commentary on the results obtained with the visual and statistical analyses, in the light of previous empirical work and the existing literature. The findings of the study must be considered within the context of the possible methodological weaknesses of this research. In particular, the performance of the diary as a research instrument will be debated and the various strategies adopted during the analysis reviewed. Finally, issues and challenges encountered whilst conducting this piece of clinical nursing research will be described.

9.2 Commentary On Results

9.2.1 The fatigue experience

Most patients had already experienced fatigue before the commencement of diary keeping (85% of subjects enrolled into the study). In just over a third of the sample, subjects felt that fatigue had worsened to some degree during the period of diary keeping, compared to the period preceding data collection. They perceived fatigue to be related to their illness or its treatment and their views reflected the literature in terms of the factors which they identified as contributory. This provided preliminary evidence of qualitative and quantitative differences in the fatigue experience prior to the onset of illness/treatment and that encountered during chemotherapy. However, there were only 26 subjects for whom this was their first pulse of this current chemotherapy protocol and thus it was difficult to quantify how much of a difference the administration of chemotherapy made to an individual's fatigue pattern. The majority of these subjects felt the extent of their fatigue had increased since beginning chemotherapy, and not surprisingly attributed this to their treatment. This question will only be fully answered in a study which recruits a large inception cohort and obtains baseline quantitative retrospective estimations of previous fatigue experiences, which facilitates comparison with any fatigue which occurs following chemotherapy administration.

Fatigue was described in terms of a subjective self-evaluation of sensations which were often diffuse, and in many patients, associated with a constellation of different feelings. Descriptors of a physical and emotional nature, as well as those related to energy level changes, were used to differentiate the sensation from tiredness. The researcher concluded that expressions of fatigue in terms of its severity and temporal, affective, sensory, evaluative and behavioural dimensions varied between individuals. This has tremendous implications when considering the best ways to assess this phenomenon, in both research and clinical practice.

Perceived causes of fatigue, from the perspective of this sample, were similar to those reported by Piper (1989), although the rank order differed. The American researcher found her sample most frequently cited changes in psychological patterns as the most common perceived cause of fatigue, but in the present study subjects most frequently attributed fatigue to treatment, changes in activity and rest and the presence of additional symptoms e.g. nausea and pain. Changes in psychological patterns were the least frequently cited. The source of data in Piper's study is not detailed, so the reason for the differences are difficult to suggest. Cultural differences between an American and British sample should not be dismissed, particularly as it has been suggested that aspects of fatigue are culturally determined. Additionally, the timing of data collection could influence response. Review of recordings in the diary suggested that subjects frequently attributed their fatigue, at the beginning of the diary keeping period, to chemotherapy; whereas other reasons were cited as diary keeping progressed. These were frequently related to the expected sequelae of chemotherapy and alterations in activity and rest patterns. Information concerning those factors to which patients attribute their fatigue is vital for the design of any successful intervention study. The importance of considering this has been argued by Wessley and his team in relation to Chronic Fatigue Syndrome (Wessely, Butler, Chalder *et al.*, 1991). It is argued that continuing attribution of symptoms to an external agent engenders a state of *learned helplessness* (Powell, Dolan and Wessley, 1990). Although cancer patients do not often attribute their fatigue to a sole external factor, such as chemotherapy, this may still influence their behaviour when it comes to self-care action. This will be elaborated on later in the discussion (see section 9.2.4).

During the diary keeping period overall 89% of the sample reported fatigue. This is a remarkably similar figure to previous estimates when cross-sectional approaches to data collection were adopted (Meyerowitz, Sparks and Spears, 1979 ; Nerenz, Leventhal and Love, 1982 ; Nail and King, 1987 ; Tierney, Taylor and Jose Closs, 1989). However, if these data are examined in greater detail, the percentage of subjects experiencing

fatigue on any single day appears to be heavily dependent on the timing of data collection - fatigue was experienced on only 47% of diary keeping days. Overall, *mean fatigue scores* are low to moderate ($\bar{x}$= 23.5), but at specific times fatigue may be severe (SD ±22) with very problematic peaks. This is valuable information for health care professionals planning patient teaching and counselling. Failure to realise differences in healthy versus cancer populations in the limited studies that have been conducted (Pickard-Holley, 1991) may be an effect of cross-sectional data collection. It is possible that the majority of cancer subjects reach a similar pattern to that of the normal population when nearing the end of a pulse of chemotherapy.

The categorisation of fatigue associated with chemotherapy as chronic, rather than acute, has received little research documentation and may be of limited usefulness. The current study, as the results reveal, lends support to a view that the majority of patients receiving chemotherapy may not suffer from chronic fatigue, but rather acute periods of fatigue. An alternative interpretation may be that some patients experience a period of acute fatigue, superimposed over a degree of chronic fatigue already present. Examination of individual time plots revealed that in some subjects fatigue scores do not return to zero over the pulse of chemotherapy. Without comparison to a matched sample of healthy subjects, it is difficult to determine whether these patients experience a degree of chronic fatigue in addition to the fatigue experienced as a result of the demands of everyday life. A comprehensive approach, in which fatigue is considered as having multiple dimensions with all the dimensions contributing to some degree, would seem more helpful than attempting to distinguish between different types of fatigue.

9.2.2 Patterns of fatigue and other daily study variables

Together, the visual and statistical analyses confirm the profound variation in fatigue, including the other symptoms and mood states that cancer patients receiving chemotherapy experience. Visual analysis of the daily data captured a variety of themes: mirror/parallel shifts, large declines and improvements, stability versus dynamism and dynamics at the opening, middle and end of the diary. By recourse to these themes it was possible to review the individual data sets. These were illustrated by reference to a number of vignettes emphasising that fluctuations in fatigue are often of great personal significance. The case of mirror/parallel shifts within the 21-day and 28-day data set were confirmed statistically in one of two ways. Firstly, the time series analysis resulted in the generation of an AR(1) model in the case of the 21 and 28-day data, and a seasonal model in the case of the weekly data. Fatigue appeared on the whole to be episodic rather than persistent, although a subsection of the sample did appear to suffer from fatigue on a

daily basis without respite. Secondly, exploration of the correlation matrix and cross-correlation coefficients of items derived from the daily diary revealed associations of varying strengths between the variables on the same day.

The four dimensions of fatigue chosen for examination in the present study exhibited similar patterns. As changes in the *extent of fatigue* occurred these were closely mirrored by comparable changes in *distress from fatigue* and the level of *interference from fatigue with daily activities/chores* and other *enjoyable activities.* However, the magnitude of scores achieved on a daily basis differed according to dimension, reflected in a respondent mean on the *extent* VAS of 26.8, versus 18.6 on the *distress* VAS, 23.7 on the VAS concerned with the degree to which fatigue *interfered with ability to carry out daily activities* and 24.4 on the VAS concerned with the degree to which fatigue *prevented subjects from doing things that are enjoyed.* Thus, the highest scores were consistently associated with the *extent of fatigue* item and lowest with the item concerned with *distress.*

Distinct patterns of fatigue emerged related to *nature of drug administration.* This appeared to influence the onset and trajectory. In particular, subjects receiving continuous chemotherapy (e.g. ECF protocol) achieved significantly greater *mean fatigue scores* than subjects receiving monthly and weekly pulsed chemotherapy. These latter groups exhibited a pattern which appeared to be strongly related to the timing of drug administration (e.g. Carboplatin and weekly 5-Fu). The onset of large declines and improvements in fatigue were frequently associated with specific times in the pulse, for example, in the days immediately following a bolus dose.

Previous researchers utilising cross-sectional designs report increased fatigue during the estimated nadir period and immediately prior to the next pulse of chemotherapy (Jamar, 1989 ; Pickard-Holley, 1991). The presence of such patterns were confirmed in this study which also provided additional information about the persistent tendency of the *mean fatigue score* and other daily variables to decrease over time (confirmed by RM-ANOVA) in subjects receiving 21 and 28-day cycle protocols. On visual inspection, it is clear that subjects receiving the 28-day cycle as opposed to 21-days experience a greater number of days when fatigue scores are low and not subject to a great deal of variation. Thus, the pattern of intensity appeared to be related to the duration of the pulse. The rise in fatigue on the days immediately before the next pulse, evident from the time plots, could be an indication of the role that expectation may play in the onset and progression of fatigue. Anecdotal remarks during interviews and telephone contact provided support that such psychological mechanisms may play a major role. Further examples of such influence can be found in subjects who perceived

that their level of fatigue had subsided with the last pulse of chemotherapy as they knew this to be the final planned administration, or that re-staging had confirmed that chemotherapy treatment appeared to be having its desired outcome.

The use of daily data in the present study gives an indication of the dynamics of fatigue between periods previously chosen to estimate fatigue, in terms of both frequency, duration and severity. The duration of fatigue for individuals shows clear inter-subject variation. A few subjects experienced a significant level of fatigue throughout the diary keeping period, whereas others appear only to have experienced a degree of fatigue for a few days. Some were not affected at all. Such patterns have implications for health professionals. Informing patients about potential patterns and assisting them to adjust activities correspondingly may help them to plan their daily activities and social opportunities. Information could also be provided concerning the most usual periods of the day when patients could expect fatigue to occur - early afternoon, late afternoon and early evening. The form of data collection used in this study did not permit recording of severity at different time periods. Some subjects who experienced particularly severe fatigue reported that they had indicated fatigue to be present all day, but within the day there were particular periods when it was more or less intense. This could be investigated in another study.

9.2.3 Associations between fatigue and the selected study variables

Most of the research concerning fatigue in cancer patients has not clearly identified specific correlates of fatigue. However, research in other populations points to correlates that may also be relevant for cancer patients. It has been suggested by a variety of authors that symptoms, side effects and medications may interact to produce fatigue. The strength of associations between fatigue and items on the daily diary in this data set all achieved significance, albeit at varying levels, but it was perhaps surprising that the smallest values were between the *fatigue* scales and *sleep* and *nausea.* The cross-correlation coefficients indicated that it was wise to consider the relationships recorded for that particular day rather than the preceding or following day. The highest scores for *nausea* were achieved immediately post chemotherapy. Those scores subsequently subsided to indicate a virtual absence of nausea as diary keeping proceeded. In the 21 and 28-day cycle, this may have influenced the level of association for this variable with fatigue when the data were aggregated. In the case of a disruption in *sleep* , described at the extreme of the VAS as "worst night possible", the results could be interpreted in a variety of ways. Firstly, previous writers may have been erroneous in their assumption that sleep patterns are in some way connected with fatigue in cancer patients.

Alternatively, the wording of this scale failed to capture a possible relationship. The second interpretation is likely as some subjects commented that they were marking the scale to reflect "sleeping as normal" which meant sleep was of a poor quality and limited quantity. A detailed investigation of sleep and rest patterns and their relationship to fatigue would appear to be warranted in this population

9.2.3.1 Demographic and treatment variables

It has also been speculated that the characteristics of patients such as age, sex, treatment response, and variables associated with the disease such as its stage, specific treatment protocols and length of therapy may affect fatigue. These factors were also explored within the current analysis.

The characteristics of age and gender did not appear to be associated with increased *mean fatigue scores* in this population. There are suggestions within the literature that women may be more prone to fatigue. Nerenz, Love, Leventhal and Easterling (1982) suggest that younger patients are more likely to report increased nausea and fatigue than older patients receiving chemotherapy. Statistical procedures initially failed to support this previous trend. However, when age groups were collapsed (under or over fifty years of age) a significant relationship became apparent between greater fatigue and the younger patients ($U=761$, $p=<.05$), but this was not duplicated with mean symptom distress scores. The explanation for higher fatigue scores in the younger age group could be two-fold. Firstly, younger patients may have greater demands placed upon them due to family responsibilities and the demands of employment. Secondly, the elderly may hold expectations that they will develop fatigue due to the combination of age and treatment/illness related factors and thus be better able to cope with any resulting fatigue, whereas the younger subjects are less able to rationalise the occurrence of fatigue and so find it more difficult to cope. The presence of a pre-existing health problem, in addition to cancer, places extra demands on an individual and might be expected to result in a greater degree of fatigue. In the current sample there was no significant association between the presence of an additional health problem and *mean fatigue scores*, although subjects on the whole considered such problems to be relatively mild.

Characteristics such as site and type of cancer, the extent of disease and length of time since diagnosis could influence the onset and *extent of fatigue*. Associations of these variables to *mean fatigue scores* were explored within the aggregated data analysis. *Site of cancer* did appear to have some influence on fatigue scores and this will be discussed below.

To facilitate comparisions between those with and without advanced disease and their corresponding fatigue scores, it was necessary to record the presence of advanced disease in the sample. This was done in a number of ways. Firstly, by recording the *presence of liver metastases*, secondly through an estimation of the *extent of disease* prior to this present course of chemotherapy (i.e. no disease, locally advanced or metastatic), thirdly by recording the consultant's opinion of the current treatment as *palliative or non-palliative* and finally by noting the *intended purpose* of this treatment (i.e. neo-adjuvant, adjuvant, for metastatic disease or for locally advanced disease when it was not considered a neo-adjuvant treatment). Analysis revealed no significant differences in the *mean fatigue scores* of subjects in these different groups. The lack of any relationship between fatigue and the stage of disease has been supported in previous research (Blesch, Paice, Wickham *et al.*, 1991 ; Pickard-Holley, 1991). This was also the case when data were examined for differences in fatigue scores associated with the length of time that had elapsed since diagnosis. *Duration of illness* on initial analysis in a mixed sample of breast and lung cancer patients, failed to correlate with fatigue in a study by Blesch, Paice, Wickham *et al.* (1991). However, when the groups were considered separately duration of illness was significant in the breast cancer subjects. The authors suggest that the lack of correlation in the lung cancer group might be because there was little variability in duration of illness in this group and because the disease is aggressive and subjects die within a short period of diagnosis, and because fatigue may be more of a problem for people who are expected to live longer with the disease. It is unlikely that such a clear relationship between duration of illness and fatigue exists.

Although limited, due to small sample size, an illustration of the impact of advanced disease on *mean fatigue scores* is possible by comparison of subjects receiving 5-Fu ± Levamisole as an adjuvant therapy or 5-Fu for metastatic disease. The presence of metastatic disease in these subjects was reflected by higher *mean fatigue scores*. However, this interpretation is confounded by the fact that those receiving 5-Fu as an adjuvant received a dose of 450mg/m^2, as opposed to 600 - 750mg/m^2 for metastatic disease. Interpretation, in the case of the other protocols, is complicated by the pairing of the site and extent of the disease with specific chemotherapy protocols. It would be valuable to consider the dimensions of fatigue within the same chemotherapy protocol but with subjects who have cancer in differing sites. However, as protocols become increasingly tailored to individual cancers this may not be possible. Chemotherapy is traditionally used in patients who have cancers acknowledged as being only suitable for palliative therapy - small cell lung cancer, stage III-IV ovarian cancer and cancers of the upper gastrointestinal tract. This was reflected in the proportions of the current sample receiving chemotherapy for what were considered palliative reasons. In recent years the

role of chemotherapy as an adjuvant therapy has gained approval, particularly in relation to breast and colon cancer. A future study should examine the fatigue experience of patients in groups such as these as compared with those receiving therapy for metastatic disease. A multi-centre study would potentially be required to attain sufficient numbers of patients to make such a comparison possible.

Given that in the present sample subjects receiving continuous chemotherapy experienced more fatigue, the recent trend to administer continuous chemotherapy via portable pumps, suggests that in the future fatigue may become increasingly common. This protocol was administered to subjects with cancer of the oesophagus, stomach, duodenum, pancreas and bile duct. It is impossible to say whether the increased fatigue scores were principally due to the continuous chemotherapy or to some other variable such as the site and/or extent of the cancer. Small sample size hampered detailed analysis of these subsamples. Only by recruiting larger numbers of subjects such as those with pancreatic cancer receiving this protocol for both locally advanced and metastatic disease would it be possible to elucidate such factors.

It was not possible to determine any significant differences in overall fatigue scores dependent on whether subjects had received previous treatment (chemotherapy and/or some other modality such as surgery, radiotherapy and/or endocrine therapy). A large proportion had not received any chemotherapy before. This was not surprising as the majority of the sample were newly diagnosed, within the previous 6 months. Although data were collected on the proximity of these treatments to this present chemotherapy, because of the small number of subjects in each group, it was impossible to analyse these data in any meaningful way.

The length of time subjects had been receiving a particular protocol, according to the pulse of treatment they were receiving, was not significantly related to fatigue. The greater number of pulses of treatment a patient had received might be expected to induce a cumulative effect in terms of fatigue. However, psychological factors, such as reaching the final pulse, may induce relief at the expectation of finishing chemotherapy. This is supported by anecdotal comments. It could also be argued that, at the beginning, patients would be learning to adapt to the demands of treatment and thus could experience a greater degree of fatigue, developing more successful coping strategies as treatment progresses. Piper *et al.* (1990) reports significantly greater scores at the beginning of chemotherapy than at subsequent treatment periods (e.g. nadirs and subsequent pulses). This finding is in contrast to a report by Pickard-Holley (1991) which failed to establish a relationship between course and level of fatigue in a small sample of women with ovarian cancer. Subjects receiving Epirubicin and Etoposide were an example of a group

where the effect of treatment on symptom distress, in particular breathlessness, is dramatic in the first few weeks of treatment. Although these patients were in the palliative phase of treatment; chemotherapy, albeit in the short term, led to a reduction in symptoms. Subjects frequently remarked that, if they had been approached earlier in their treatment, the level of fatigue and the close association with the symptom of breathlessness, would have been much greater. The relationship of breathlessness with fatigue has been explored (Brown, Carrieri, Janson-Bjerklie *et al.*, 1986) and people with lung cancer have been reported to confuse the two sensations frequently.

9.2.3.2 Symptom distress

Tiredness was reported to be the symptom causing the greatest magnitude of symptom distress as measured by the HSDS. This finding is supported by previous studies (Knobf, 1986 ; Strauman, 1986 ; Rhodes, Watson and Hanson, 1988) and it replicates the findings of Holmes (1991). Similarly subjects commonly reported significant distress through an inability to concentrate, mood changes and alterations in appearance. However, overall, the mean ratings for all items indicated a relative lack of distress and in just under 40% of the HSDS completed, subjects did not suffer significant distress from any of the listed items. Other researchers have confirmed that it is usual for average ratings of items on symptom distress scales to be mild to moderate (Knobf, 1986). Estimates of fatigue and symptom distress may be underestimated as these exclude patients who did not complete items on a number of days, either through illness or refusal to participate.

Lower symptom distress scores (i.e. an indication of greater symptom distress), as measured by the HSDS, were highly correlated with *mean fatigue scores*. This association was confirmed by the Mann-Whitney procedure. Most of the individual items (except *nausea*, *sleep* and *diarrhoea*) on the scale also achieved significant relationships with *mean fatigue scores*. Some of these associations would be accounted for since one of the items on the HSDS is concerned with tiredness. However, when this test was repeated with the tiredness item omitted, the result remained significant. It may thus be concluded that a relationship exists between some of the distressing symptoms accompanying cancer and its treatment and fatigue in this sample. However, *nausea* and *sleep* fail to demonstrate consistent association with the *mean fatigue score* within both the repeated measures and the daily data set.

Subjects with a diagnosis of pancreatic cancer receiving the bolus and continuous regime of ECF, or subjects with an unknown primary receiving Cisplatin and 5-Fu, clearly experienced significantly greater symptom distress than subjects in the remaining

diagnostic groups. *Diarrhoea* was a particular problem for subjects receiving weekly injections of 5-Fu and oral Levamisole. Subjects reported that episodes of *diarrhoea* coincided with the ingestion of Levamisole tablets. Higher levels of symptom distress were experienced by subjects who were undergoing the first pulse in a course of chemotherapy. In this sample indicators of advanced disease were not associated with higher levels of symptom distress.

When subjects were asked to record the presence of additional problems there was a significant relationship between their presence and greater *mean fatigue scores*. This must be interpreted with caution as those subjects who recorded an absence of fatigue were not given the opportunity to complete this item. However, this finding supports the other results concerned with the association between symptoms and fatigue.

The onset of significant health changes throughout the diary keeping period was ascertained at the final interview. Such health problems appeared to contribute significantly to increased fatigue scores. Alteration in the body's immune status caused by bone marrow depression and which contributes to infection and fever were largely responsible for such problems.

9.2.3.3 Mood

The consensus from the literature reviewed suggests that levels of psychological distress and mood state are potentially important variables to consider when examining fatigue in cancer patients. Aspects of negative affect (e.g. anxiety, depression, anger) have all been associated with the experience of cancer, although the universality of the association of anxiety, depression and hostility with a diagnosis of cancer has been challenged. Mood disturbances have also been associated with fatigue in the general population (Chen, 1986, for example) and people with cancer (Blesch, Paice, Wickham *et al.*, 1991).

In the present study relatively low levels of mood disturbance were indicated by the scores achieved on the MACL and an absence of anxiety and depression predominated in the sub-sample completing the HADS. These findings are consistent with the results of previous research with the MACL in a group of cancer patients (Dawson, 1991) and mixed groups of medical patients (Openshaw, 1984). Several investigators who have employed the Profile Of Mood States (similar to the MACL) have reported a low incidence of psychological symptoms within their samples (Plumb and Holland, 1981 ; McCorkle and Benoliel, 1983 ; Cassileth, Lusk, Brown *et al.*, 1985). Within the present sample there was almost a complete absence of any variability in the

tension-hostility domain, whereas the other domains exhibited some degree of change. People differ widely in their emotional responses to cancer. There were negligible proportions of the sample who reported a high level of mood disturbance. However, this was more evident at the beginning of the diary keeping period, immediately following chemotherapy administration. Over time only the scores of the subjects receiving a 21-day cycle of chemotherapy on the scale concerned with *depression-dejection*, achieved significance, as assessed by the statistical procedure, RM-ANOVA. Conversely, both the VASs concerned with mood achieved significance in this group. This was not the case in subjects receiving a weekly cycle, nor in the 28-day group. However, a trend was evident in the scores of the latter group, although it did not achieve statistical significance. Subtle shifts in affect may not be detected through the mood questionnaire which employed ordinal scaling, but they were evident in the trend observed through visual analysis of the VAS items concerned with mood. The pattern of mood disturbance mirrored that of fatigue.

The relationships between demographic/medical variables and mood state were explored in conjunction with scores achieved on the MACL, the item concerned with mood on the HSDS and the bipolar mood VASs in the diary. As with fatigue, disturbed mood scores were significantly greater in the pancreatic cancer group, subjects receiving the ECF protocol and by the bolus and continuous route. Subjects who had not received previous treatment for their cancer recorded higher scores on the *anger-hostility* and *depression-dejection* subscales, perhaps indicating that they had not yet adapted to the experience of treatment; although there were no significant findings when the scores were examined by length of time since diagnosis. A certain lack of consistency in the results was evident. For example, subjects receiving palliative chemotherapy attained higher scores on the *depression-dejection* subscale but no relationship was apparent when scores were examined in conjunction with the other indicators of advanced disease: the *presence of liver metastases* and *disease status*, or in relation to scores on the VASs and the HSDS item. Sporadic differences were as likely to be due to chance as to any systematic factor, given the multiple tests performed. Few systematic differences in POMS subscale scores have been observed across the sites of cancer in the studies mentioned previously, with the exception of those with pancreatic cancer (Cella, Tross, Orov, Holland, Silberfarb and Rafla, 1989). This condition is associated with increased risk of depressive symptomatology (Holland, Korzun, Tross *et al.*,1986).

Relatively strong correlations were obtained between the mood items in the daily diary (the bipolar scales of *calm-anxious* and *happy-sad* and a unipolar scale concerned with *concentration*) and fatigue scores. As fatigue scores increased there was a tendency towards anxiety and sadness and decreased ability to concentrate.

All five mood factors on the MACL achieved significant associations with *mean fatigue scores* in the expected direction. Utilising the maximum score recorded across five and three scales (in the latter *vigour-activity* and *fatigue-inertia* items had been removed from the analysis) revealed that negative affect, as indicated on one of the three scales : *tension-anxiety, depression-dejection* or *anger-hostility*, was related to significantly higher *mean fatigue scores*. The present analysis is consistent with previous studies where the POMS (original and shortened form) was utilised (Jamar, 1989 ; Piper, Lindsey, Dodd, Ferketich, Paul and Weller, 1989 ; Blesch, Paice, Wickham *et al.*, 1991).

The results from the HADS confirmed this relationship: *normal* scores on the anxiety and depression subscales were associated with lower *mean fatigue scores* in the subsample completing this instrument at the close of data collection. However, whether the presence of negative affect precipitates fatigue or the presence of fatigue induces negative affect remains unclear. Studies employing longitudinal data collection will be required to disentangle this relationship. Fatigue is unlikely to be the sole factor accounting for psychological distress related to treatment. The influence of positive affect, including adjectives to reflect enthusiasm, determination and mental alertness as well as energy, rather than just the absence of feelings of anxiety and depression may also be important to consider in future studies. Researchers should also consider the symptom perception hypothesis of Watson and Pennebaker (1989) which purports that individuals differ in how they respond to, or complain about, body sensations. The symptom perception model posits that the association between negative affect and health complaints is spurious; reflecting that high negative affect subjects are more likely to attend to or complain about physical sensations. It has been suggested by Sensky (1990), following a review of research on patients' reactions to physical illness, including cancer, that whether or not a patient becomes depressed or anxious is only weakly associated, if at all, with the severity of the condition or its physical manifestations. What seems to matter most are the individual's attitudes to, and thoughts and beliefs about, illness. It is suggested that future studies should explore and describe cognitive factors, as well as psychological distress, as these may play a role in the development and progression of fatigue.

9.2.4.4 Section summary

From the above discussion, it is apparent that differences in fatigue scores between groups of cancer patients cannot be categorically related to the factors chosen for examination in this study. It is most likely that a number of causal and mediating factors

are implicated, and that their relative influence varies between individuals. A constellation of demands exist for a person dealing with the experience of cancer and its treatment. The incidence and severity of fatigue may not solely depend on the disease or treatment employed. Rather, it is suggested that the nature and *extent of fatigue* depend to a considerable extent on the individual concerned. Findings indicate that, although overall fatigue may be similar between chemotherapy groups, there is considerable individual variation in the *extent of fatigue* and the amount of associated *distress*. A recent report (Lee, Lentz, Taylor, Mitchell and Woods, 1994) asserts that fatigue is an indicator of adaptation, and may be examined in relation to internal and external environmental demands. This model could usefully be adapted to explore the individualised response and the antecedents of fatigue in cancer patients. Variability in scores may be explained by the manner in which subjects' cancer and its associated symptoms impinge and coincide with positive and negative life events and may be modified by the degree of social support they receive. Certain aspects of lifestyle, such as diet and successful balancing of activity and rest, may be important to consider along with degrees of effective social support.

In conclusion to this section, it would appear that interpretation of these data is difficult due to the interdependency of multiple variables. Clearly there are some strong influencing factors, for example, the pancreatic cancer patients who receive the ECF protocol consistently record greater fatigue scores. This is supported by clinical evidence. Pancreatic carcinoma is particularly aggressive resulting in high levels of symptom distress. There seems to be sufficient justification to assert that variation is present according to site and type of protocol employed. However, multifaceted correlations between symptoms, mood and fatigue exist and are difficult to disentangle. Testing theoretical relationships through statistical analysis has not been straightforward and this difficulty was magnified by within-individual variability confounding the analysis of between-subject variability.

9.2.4 Self-care

Subjects were resourceful and inventive in the selection and performance of self-initiated interventions in response to fatigue. A number of commonly recurring themes were evident, but as in previous studies, interventions listed were only partially effective (Nerenz, Leventhal and Love, 1982 ; Dodd, 1988 ; Rhodes, Watson and Hanson, 1988 ; Piper, 1989). On a large proportion of diary days, when fatigue was experienced, self-care behaviours failed to be initiated. Further work is required to differentiate between proactive versus reactive interventions as the nature of behaviours is not clear from these

data. In future studies, subjects not experiencing fatigue could be asked whether they initiate preventive activities and the nature and effectiveness of these. The most common behaviours listed were, not surprisingly, rest and napping which could be seen as both proactive and reactive actions, so further elucidation is important. It has traditionally been acknowledged that chronic fatigue is often not experienced in relation to some form of activity and exertion; and thus fatigue, which is chronic in nature, would not be expected to be completely dispelled by methods which entail taking adequate rest and sleep.

Higher *mean fatigue scores* appeared to be associated with the performance of *self-care* in the sub sample of subjects who experienced fatigue. However, when the relationship of individual fatigue items to *self-care* were examined, the occurrence of significant relationships with each of the four scales were not consistent. Significant results related to the scales concerned with the degree to which fatigue *interfered with daily activities/chores* and *interfered with engaging in activities which were enjoyed*, rather than to the scales concerned with *extent* and *distress* from fatigue. This may indicate that subjects will initiate self-care behaviour according to the degree to which fatigue impacts on daily household and social activities.

A more complex relationship between self-care and fatigue is likely in addition to the above explanation. Rhodes, Watson and Hanson (1988) discuss the concept of meaning in relationship to the existence of a symptom and the relation of this to self-care. They purported that an individual with symptoms due to illness (weakness and tiredness are listed as examples) modifies behaviours in an attempt to maintain normal self-care function and valued activities. Whereas, they suggest that, symptoms which are disease or pathologically orientated (such as nausea and vomiting) frequently have prescribed medical or nursing interventions and hence are viewed differently. The individual with symptoms, believed to have resulted from a disease condition, is considered sick and therefore may have fewer incentives to engage in self-care behaviour. In other words, the meaning assigned to a symptom may interact with the individuals ability to engage in therapeutic self-care activities.

Data from the current study indicate that most patients consider fatigue to be associated with the disease and its treatment. Following the argument above, these patients would be less likely to perform self-care. Health care professionals may intensify this interpretation when they attribute fatigue to the chemotherapy. Patients undoubtedly assign different meanings to the symptom of fatigue depending on whether they consider it to be generated through *illness* or *treatment* and there is likely to be considerable variability in this over time. This will influence their ability to perform self-

care. Anecdotal remarks during the interviews, when subjects were asked about self-care and fatigue, lend support to this.

The Common Sense Model (also known as the Self-Regulatory Model) has been used to study self-regulation in a number of chronic illnesses including cancer (Ringler, 1983 ; Leventhal, Easterling, Coons *et al.*, 1986, for example). It is an information processing model in which individuals are seen as motivated to construct meaning for body sensations, in order to engage in self-regulating behaviours. A central feature of the model is the assumption that processing occurs in three stages : representation, coping and appraisal (Leventhal, Meyer and Nerenz, 1980). They suggest that at any given time that processing is multistaged, hierarchical and parallel (Nerenz and Leventhal, 1983). Considering the former discussion, this model could be exploited to study fatigue and associated self-care processes and inform nursing practice. In particular, the way in which a representation of the symptom is formed from sensory experience, how an existing representation influences the reporting of fatigue, and how representation is linked to coping with this might be explored.

Data concerned with patients' reasons underlying their choice of strategies would be valuable, as would the processes of problem-solving when those behaviours first chosen appear ineffective. The value subjects in this study placed in preserving normality was striking. Interventions appear to be active and/or passive. Active implies that they are deliberate and purposeful and specific to the relief of fatigue; whereas passive intimates that they are inherent in everyday activities and almost certainly familiar and well known to the subject. Whether or not cancer patients feel they can and should attempt to influence the course of their fatigue needs to be ascertained. Remarks from subjects during the current study led the researcher to consider that this might be a crucial consideration in the design of any intervention study, aimed at ameliorating fatigue through self-care. Interventions that are congruent with, rather than antithetical to, patients' own beliefs are more likely to be successful.

Subjects frequently only listed one, rather than a combination of behaviours. A few subjects performed multiple self-care behaviours, and it would be interesting to explore the characteristics of such people in more detail. The lack of a high degree of distress resulting from fatigue may account for the moderate level of self-care activity. At present it appears that patients receive little advice and support from health care professionals as evidenced by the absence of recordings concerned with the source of ideas for action from this quarter. This has been noted in previous research in relation to symptom management after cancer therapy (Dodd, 1986).

9.3 Limitations of the study

In the current study many of the problems detailed in the literature, associated with measuring subjective variables and perceptions, were encountered in the process of obtaining estimates concerned with fatigue and other related variables over time. These were exacerbated by the need to obtain information at a time when patients were particularly likely to be under stress and sensitive to questions relating to illness and its treatment. It is clear that often the most theoretically interesting questions and relevant to the practitioner rely on data that is difficult to collect. Methods to address theoretically interesting issues often strike emotionally distressed cancer patients as irrelevant to immediate needs and experiences. This particular piece of clinical research had to involve a number of compromises in the face of such challenges.

9.3.1 Design

The collection of data on a daily basis is an advance on the cross-sectional designs previously used. However, chemotherapy patients were not identified at a uniform stage of the treatment cycle and any descriptive study is limited in its ability to detect causal mechanisms. The inclusion of a control/contrast group would have improved the strength of the design. It is difficult to report with certainty that the fatigue patterns observed were due to illness and/or treatment effects. However, the magnitude of fatigue in the period post chemotherapy and the manner in which the pattern mirrors the sequencing of administration provides some evidence for a link. Crosby (1991) questions the validity of comparing healthy subjects with those who are ill, as there is no evidence that the feelings associated with a normal daily routine are the same as those associated with a chronic illness. The present study provides some tentative evidence that the feelings and nature of fatigue may differ between healthy subjects and patients with cancer. More qualitative approaches using interviews would provide further information and perhaps differentiate the fatigue experience of people with cancer undergoing treatment from that fatigue encountered as a function of normal daily life.

The recruitment of an inception cohort followed by longitudinal follow-up has been considered an important design consideration (Irvine, Vincent, Bubela *et al.*, 1991). Especially as the lengthy and changing nature of a chronic disease such as cancer and its treatment compound the difficulty of developing an integrated view of fatigue and any associated variables. For example, theoretically subjects receiving later pulses of chemotherapy may be in better health and less fatigued than those mid-way through treatment due to eradication of their cancer. Conversely, these subjects may have

experienced increasing toxicity or extension of their disease and be experiencing increasing levels of fatigue. It proved difficult to recruit subjects at the beginning of their first pulse of chemotherapy in this study and it may be more realistic when designing studies that require an inception cohort to recruit them a few days following their first experiences of therapy. Patients could be asked to reflect on their recent experience before proceeding to prospective data collection. It is important to determine how comparable the individuals remaining in the study are to those who drop out or fail to maintain a complete data set. Clear records were kept in the current study of an individual subject's progress through data collection. This would be even more vital if the period of data collection was extended. Results may be skewed to reflect the fact that those with fewer disruptions and less functional compromise are able to complete the diary task. If this is the case, the percentage experiencing fatigue will have been underestimated. This will be discussed further below.

9.3.2 Sample, subject accrual and attrition

Sample size is acknowledged as a constant problem throughout clinical nursing research (Dixon and Moritz, 1983). The present research emphasised this difficulty although the researcher attempted to enrol all patients who met the criteria as they became available. The availability of subjects had been assessed during the design phase. Record reviews were encouraging and unit personnel were asked about any projected changes. Access to patients was limited by both formal and informal restrictions. As detailed in Chapter 5, the tight sample criteria had to be loosened, as the study progressed, when accrual proved slower then expected. This late decision meant potential subjects had been missed earlier in the study. Further reductions in the sample occurred at induction to the study. As the study adopted a longitudinal design, it had been anticipated that the loss of subjects over the course of data collection would reduce the final sample size. Attrition was encountered at various stages of data collection. Subjects failed to start the diary keeping task despite agreement and others discontinued at a later stage. An investigation of potential sources of bias was only possible through recourse to demographic and medical variables comparing responders with non-responders. Beginners, non-beginners, completers and drop-outs were compared. No significant differences were revealed when the selected demographic and medical variables were considered. Little comment has been made in the literature about the characteristics of successful diary keepers, although a report by Carp and Carp (1981) related attrition in diary keeping in a healthy population of commuters to low income, little education, minority ethnicity and poor health. The number of subjects experiencing major toxicity resulting in a period of hospitalisation or physical/mental deterioration, making it difficult for them to complete the diary, was not

unreasonable, considering subjects were in the active phase of cancer treatment. However, loss of subjects may have resulted in a selection bias that may have ultimately skewed the findings.

The introduction of experimental chemotherapy protocols for some of the cancers included in the study, during the data collection phase, also had the effect of reducing the available sample. For example, 12 months into data collection, ovarian cancer patients were given the opportunity to enter a trial if they had not received previous treatment and those randomised to the experimental arm were lost as potential subjects. The strategy of using more than one hospital was considered but rejected due to the manpower requirements. Instead the data collection period was extended.

9.3.3 Fatigue measurement

A number of different approaches were selected to describe the subjective dimensions of fatigue in the current study: onset, pattern, duration, intensity, and distress. The issues relating to the Piper Fatigue Scale will not be revisited here: the reader is referred to Chapter 5 for a discussion of the researcher's experiences using the scale within the context of the current study. Overall, there was a satisfactory level of instrument convergence in relation to the items selected to measure the construct. However, certain recordings, by a number of subjects, raised debate about how subjects were conceptualising and hence reporting their feelings about fatigue and tiredness. This was supported by their responses in the preliminary interview to open questioning concerned with whether they considered the feelings of tiredness and fatigue to be different or the same. A number of individuals discriminated between tiredness and fatigue as constituting different experiences and this was reflected in their completion of the MACL, the VASs in the diary and the HSDS. Researchers need to consider, in greater detail, the measurement of subjective states and, informed by the literature, consider whether such concepts as vitality and fatigue should be placed on the same continuum. Research by Lee and co-workers suggests this may not be the case (Lee, Lentz, Taylor *et al.*, 1994).

The instruments and approaches selected to assess fatigue in the present study are well accepted and are accorded with an acceptable level of reliability and validity. The manner in which this experience has been represented in the literature by quantitative measurements may have resulted in limited understanding of the actual nature of the experience of fatigue. The complex nature of the phenomenon, which is being suggested by this and other studies, should lead to further study adopting qualitative research

approaches. The sensitivity of research instruments should also be considered, especially their ability to detect subtle variation in feelings, both physical and mental, and relate these to changes in fatigue states.

The present study offered a methodological advance over previous designs because it documented the patterns of fatigue in relation to treatment. However, it is still possible that fluctuations in fatigue escaped detection, though significant to individuals concerned, owing to lack of sensitivity of the instruments. It is clear that data sets containing repeated measures are required, supported by the continued development of methods most sensitive in revealing patterns of change. The interview demonstrated the importance of collecting repeated measurements of fatigue to gain an accurate representation of its temporal pattern. The waxing and waning of fatigue over time, demonstrated by the responses of subjects who had been fatigued at the beginning of a course of chemotherapy, but who were free from fatigue at the point of data collection, were difficult to represent within a rigid coding system, becoming meaningless when too many categories were introduced.

The discriminant abilities of the four VASs in the diary concerned with fatigue were moderate. The intensity and distress dimensions of fatigue appeared to have different slopes. Subjects generally rated the intensity of the sensation and unpleasantness differently, whereas the degree to which fatigue was reported to interfere with everyday and social life was similar. The results of all four VASs were highly correlated. Thus the use of a respondent mean score was justified when interpreting the results.

A number of subjects alerted the researcher to the fact that *response shift*, as described by Breetvelt and van Dam (1991) may have occurred on occasions. This occurred particularly in relation to the *sleep* and *appetite* items in the daily diary. An adjustment had taken place regarding what should be considered *normal* for a subject at that point in time rather than earlier in the subject's illness/treatment career. When subjects commented on this they were asked to mark the visual analogue scale in relation to their pre-illness status. The use of *then*-ratings has been advocated in the literature (Howard, Schmeck and Bray, 1979). Here subjects indicate, in retrospect, how they would have rated their state before treatment. It is suggested that the *then* pre-treatment scores are assigned from the same perspective and that they are therefore free from *response-shift* bias. Further research is needed to indicate the applicability of techniques for the assessment of *response shift* with regard to symptom reporting, and more specifically in relation to fatigue.

9.3.4 Aspects related to the performance of data collection instruments

9.3.4.1 The diary as a research instrument

The decision to use the diary as a data collection method was guided by the nature of the research questions. The diary provided subjects with a mechanism to provide data on a daily basis, which could be quantified to allow for both within and between-subject comparisons on the variables of interest. The method of data collection had to be acceptable to the participants. A review of the literature and previous experience with this method indicated that the diary would fulfil these criteria. Issues considered within the literature on the use of diaries as a strategy for data collection include respondent co-operation, quality and validity of data collected, concerns about the complexity of analysis and the costs associated with data collection and analysis. These will now be addressed in the context of the current study.

Process of diary implementation

The structured diary served as the primary method of data collection. Interviews were also conducted, before and immediately following, diary keeping to facilitate the process of data collection. The initial interview occurred at enrolment to the study and involved a discussion of the purpose and process of diary completion. The second interview occurred immediately following completion of the diaries and involved exploration of how subjects had found the task of diary keeping. In addition an important goal of these interviews was to ascertain the extent of any changes which may have occurred in subjects' personal and health circumstances during the diary keeping period, which may have influenced their experience of fatigue. The diary proved to be a useful way of tracing the selected variables and dimensions of fatigue. Diary training was vital to reduce errors and ambiguous entries. It was particularly valuable for those subjects who remained in hospital to receive chemotherapy. These subjects were able to meet with the researcher who reviewed diary completion and reinforced the correct method. This was more difficult by telephone, particularly if there was a problem in completing the visual analogue scales.

Completeness and quality of data

The diaries provided a detailed record of fatigue, selected symptoms/mood state and self-care behaviour, which for most subjects was continuous. Given that subjects completed their diaries mainly at home without supervision, and were very unwell, there were several threats to the completeness of the data. Incomplete diaries were returned. For

example, pages were not filled out, items omitted and entries were unclear. Poor calibre of the data may have resulted from participants' motivation to record and complete the study. Efforts to minimise these threats included the structured format of the diary (acknowledged in the literature as being more successful when collecting information about symptoms), the use of the pre- and post interviews to clarify issues regarding diary keeping and telephone contact with the subjects shortly after they had commenced the task of diary keeping. The commitment of subjects to completing the diary keeping task was impressive. In fact a number of subjects annotated their diaries extensively, wishing to provide additional information and clarify their recordings

Family members were known to have helped a number of subjects to complete the diary, especially during periods when the subject's health deteriorated. In future studies the inclusion of the question "Is somebody helping you fill out this diary today ?" may help to identify the source of the information. Use of other people to report symptoms when symptom levels escalate has been addressed infrequently, but this is precisely the time when measurements are needed and the patient is most unlikely to provide them. Fayers and Jones (1983) comment that if the assessor is a close relative of the patient and is responsible for reporting the patient's quality of life, problems may result from confounding of the patient's view and the views of the observer. However, Nixon and Bethell (1974) note that relatives are more likely to volunteer information and be empathic about changes in health than patients themselves. Patients characteristically tended to minimise and rationalise symptoms or attribute them to the inevitable consequences of ageing.

Subject co-operation

The responses of subjects during diary completion were positive. On the whole subjects responded enthusiastically when asked to participate in the study. Where the researcher sensed ambiguity, subjects were reassured that it would not be detrimental to their care if they declined to participate. Seventeen subjects declined at this time and a further twenty did not begin the diary keeping task for a variety of reasons. These have already been detailed in Chapter 6. Some of the subjects, who refused to take part, explained that they did not wish to reflect on their circumstances over a protracted period of time. The desire not to dwell on their cancer was strong in these subjects . In essence they wanted to leave their cancer in hospital, separating the role of chemotherapy patient from their other roles. Such attempts to minimise the intrusion of treatment, side effects and symptoms, by declining to elaborate or participate in longitudinal research, has also been encountered by Leventhal *et. al* (1986). Talking in an interview may have been more acceptable for these subjects. In contrast a number of subjects commented on the benefits they had

experienced through keeping the diary, including the opportunity to reflect on the number and kind of activities they performed. More generally the process of diary keeping helped them to rationalise the experience of chemotherapy.

Concerns about diary design

The researcher was concerned when selecting the items for inclusion, in the first part of the diary, that those chosen may not have reflected the concerns of paramount importance to subjects, although they had been suggested in the literature to be key dependent and/or intervening variables in relation to fatigue. However, responses to the HSDS provided evidence that changes in *concentration* and *mood* were frequent causes of distress and no further items were mentioned in sufficient numbers to lead the researcher to conclude that a vital item had been omitted. Subjects with small cell lung cancer mentioned the symptoms of dyspnoea and cough on a regular basis. Future research should include these items when examining fatigue in this population. Dyspnoea and fatigue have also been suggested to be closely related in those with congestive cardiac failure (Schaefer and Potylycki, 1993).

It is difficult to judge whether the activity of maintaining the diary sensitised subjects to the presence of fatigue. It may have been useful to ascertain whether subjects considered that, by maintaining the diary, they had been made more aware of fatigue and other symptoms. If sensitisation is present, researchers need to examine results to identify the characteristics of people reporting increased awareness. If these are present the data may need to be adjusted with statistical techniques.

The section in the diary requiring subjects to report other symptoms or problems was not particularly successful. The feature of *telescoping* was evident where continuous symptoms tended to be reported inconsistently. The final interview often revealed that this had occurred when subjects revealed the presence of minor but continual irritations of various kinds, but there were no or few recordings to reflect this. Further evidence that this occurred was provided when subjects reported that a symptom, that had been present for the previous few days, had improved, although there was no record of it in the recordings for the preceding days. Often subjects recorded no more than a few symptoms, but they were obviously of key importance to the individual. The current study supported Verbrugge (1980) in his assertion that the diary is not the best choice of instrument (when compared to interview with extensive probes) for chronic conditions with low impact, but are considered suitable for eliciting reports of acute conditions and diffuse symptoms. Solutions might include ascertaining a baseline in terms of the

presence or absence of symptoms and asking subjects to reflect each day if there had been any change or asking subjects to reflect over a week rather than daily.

The VASs performed satisfactorily in the current study. However, there still remains a need to explore the psychometric properties of VASs in more detail in relation to fatigue. Aspects of reliability need to be documented for concepts which are dynamic and subjective in nature. Internal consistency between the four VASs chosen to measure fatigue was high in the current study. It is recommended that the VAS should not be used as a single measure, but in conjunction with other instruments reflecting the multidimensionality of this concept. However, researchers should recognise that this increases respondent burden. They should probably be considered a relative, rather than an absolute measure, as such scales are not interpreted in the same manner by all patients. However the same could be said for numerical and graphic rating scales when considering subjective symptoms. At least the VAS has the advantage of being more sensitive to small changes.

There were a small number of cases of inaccurate completion. If patients understood the instructions poorly they would circle comments at each end of the line, make several marks on the line, or make marks which bore little or no relation to the line. Ganz, Haskell, Figlin, La Soto and Siau (1988) have reported problems of this nature.

In relation to self-care, even with a prospective instrument such as that employed in the current study, subjects may not have recognised or recalled activities that they used or may have limited reports to those that were considered effective or differed the most from usual activities. This may account for the relatively low number of activities recorded in the diary.

A few subjects used multiple combinations of self-care activities, but the methodology employed in this study did not lend itself to measuring the efficacy of combinations of self-care activities. The sequencing of self-care may be important and efforts to distinguish between the performance of preventive and reactive self-care, in future research, would yield valuable information. It is likely that respondents develop intricate repertoires of strategies to reduce fatigue, as well as to provide them with a perceived sense of control in relation to their fatigue.

Issues of definition

A further threat to the quality of data concerned the definition of fatigue. The researcher did not define fatigue for participants. Rather, participants' own descriptions provided

the definition of the concept. These were ascertained at the preliminary interview when patients were asked to state whether they thought there was a difference between tiredness and fatigue. When comparing between-subject scores this may be a concern. However, as reported in Chapter 6, there was consistency in the interpretations of fatigue and tiredness at the preliminary interview. Future research should explore in greater detail the nature of the fatigue experience in this population and seek to develop measures which allow the respondent to characterise their fatigue, by selecting alternatives from a broad array of descriptors, such as that utilised in the McGill Pain Questionnaire (Melzack, 1975). This may prove to be a viable method in defining what exactly the term 'fatigue' means to cancer patients.

In summary, the present study has supported previous researcher opinion that diaries are an effective means of collecting extensive data related to symptoms and the related self-care behaviour. The researcher's concerns about participant co-operation and quality of data yielded, whilst not proving entirely unfounded, did not jeopardise the study. The use of diaries in this study proved to be a user-friendly, practical, and productive method of collecting data. The evidence suggests that when cancer patients are fully informed about the requirements of the study, are monitored, and supported throughout the process of diary keeping, they value their participation and produce valid and reliable data.

9.3.4.2 Instruments used at 7-day intervals

Several instruments were used at 7-day intervals throughout diary keeping. It was intended that these would complement and extend the data collected on a daily basis, particularly in relation to mood and symptom distress. On the whole these instruments performed satisfactorily but a number of issues are worthy of mention, notably the results of the factor analyses . The implications of these results ,when inferring the presence of acceptable estimates of validity and internal consistency, are considered below.

Mood

The MACL was selected for the measurement of mood state because of validity inferred from the development of the measure by McNair, Lorr and Droppiman (1992 revised) and Lishman (1972) and its use in previous studies concerned with the measurement of fatigue (Piper, Lindsey, Dodd *et al.*, 1989, for example). Wilson-Barnett (1977) found the MACL sufficiently sensitive to detect changes in mood over time.

The MACL requires recollection of a range of feelings over the period of a day, sometimes yielding marked fluctuations. A number of subjects commented on such fluctuations in relation to their own feelings. They were encouraged to complete the instrument reflecting the emotions they had experienced for most of the day. Openshaw (1984) suggested a specific time for the assessment of feelings if a significant change had occurred during the day. This strategy was not adopted in this study. The researcher wanted to reflect the experiences of a particular day, as the fatigue VASs with which the MACL subscales were correlated, reflected the amalgamated perceptions of the individual. A patient's self-report was considered to be the truest reflection of their experience.

The use of a range of similar adjectives to describe the concept of fatigue were adopted to minimise the potential effect of the differential use of language between individuals. Barofsky and Legro (1991) suggest that research on fatigue may be confounded by the imprecision often evident in the measurement of this concept The calculation of correlation coefficients permitted an analysis of similarity of use for the adjectives employed, particularly in terms of the *fatigue-inertia* and *vigour-activity* subscales of the MACL and the fatigue VASs. As predicted the *vigour-activity* items were inversely correlated with items on the *fatigue-inertia* subscale. Moderate to strong and significant correlations were obtained between MACL subscales and the fatigue VASs. The correlation coefficients were consistently lower in relation to the *vigour-activity* subscale, in contrast to the *fatigue-inertia* subscale. As discussed earlier by Lee, Lentz, Taylor *et al.* (1994), it may be inappropriate to consider fatigue and vigour on the same continuum. As reported in Chapter 8, the MACL appeared to be measuring five relatively independent concepts successfully. This finding is supported by the previous work of McNair and Lorr (1964) Wilson-Barnett (1977) and Openshaw (1984). The overall performance of the scale in estimating mood disturbance was acceptable in this sample.

Subjects consistently failed to record variation on the *anger-hostility* subscale leading to concern that scores on this subscale may have reflected reactions to the terms listed rather than a particular mood state. This was apparent in a small scale study of ovarian cancer patients by Dawson (1991). Subjects may have been under reporting psychological distress, possibly because this effect may be associated with social desirability, particularly if they were sharing their recordings with members of their family. They may not have wished to expose their loved ones to the full extent of their feelings. The lack of published norms for different populations is problematic when attempting to interpret the scores achieved on the MACL. The results from the factor analysis and computations involved in calculating the Cronbach's α revealed that, if the

resentful and *spiteful* items were removed from the *anger-hostility subscale,* this would increase the value of Cronbach's α from ".66" to ".69" or ".68" respectively; resulting in removal of the factors which failed to achieve the highest loadings. Some subjects commented that they perceived the terms *anger* and *furious* to be identical. *Anger-hostility* was the fifth and final component extracted during the extraction phase of factor analysis and, only accounted for 4.6% of the variance.

It was problematic that, in the MACL, people who are physically ill may have utilised items on the *fatigue-inertia* and *vigour-activity* subscales to represent physical rather than affective responses. The MACL is intended to measure affective states, not energy levels. Future research should explore, in greater detail than was possible in this study, the relationships between perceived energy levels and feelings of fatigue in the cancer patient population. The *shaky* item on the *tension-anxiety* subscale could easily be misinterpreted to be a descriptor of a physical state such as the tremor associated with Parkinson's disease or related to the administration of certain anti-emetics. Findings related to the factor analysis confirmed this finding. The lowest loading on the *tension-anxiety* subscale yielded a value of ".38". The poor performance of this adjective has been described in previous studies (Wilson-Barnett, 1977). It would now appear justified to delete this item from the scale and perhaps consider insertion of an alternative adjective, such as 'anxious'.

Cancer patients rarely experience mood states in isolation. The high degree of correlation between items confirmed this. However, the independent factor structure justifies the use of this instrument to discriminate between the discrete affective states purported to be related to fatigue in cancer patients. Researchers who select the MACL for measuring purposes should consider utilising the same layout as found in the HADS. This format may reduce the tendency of subjects to omit items due to skipping a line. This sometimes accounted for missed items in the current study. Further detailed evaluation of the performance of the MACL in contrast to the HADS is necessary. However, if the researcher is principally concerned with anxiety and depression, rather than a broader spectrum of mood state, the HADS may be preferable because it does not incorporate somatic items. Caution is required as the results of the factor analysis with the small sub-sample who completed this instrument raised further doubt. This supports the results reported by Razavi, Delvaux, Farvacques *et al.* (1990) which revealed the absence of two underlying factors corresponding to the subscales of the HADS. The results of the current study add impetus to the debate concerning the separate existence of anxiety and depression: on the MACL the items *unhappy* and *depressed* were more highly loaded on the *tension-anxiety* subscale than the *depression-dejection* subscale.

Symptom distress

The HSDS selected for the measurement of symptom distress was confirmed as both a valid and reliable instrument for use with cancer patients. Despite analysis pursuing a number of different strategies, the original factor analysis of Holmes (1989) utilising a principal components approach could not be replicated. Groups of symptoms were identified, but not in the same dimensions as those identified by the previous researcher. However, as in the previous research, most symptoms were highly inter-correlated and contributed significantly to the total symptom distress score and internal consistency was high. Differences in factor structure may be the result of differences in the nature of the samples in the two studies. Holmes recruited a heterogeneous cross-sectional sample of cancer in-patients and it is not clear if they were in the process of receiving treatment. In the current study all subjects were receiving chemotherapy and most were out-patients. Further studies have been conducted by Holmes (1991) with both chemotherapy and radiotherapy samples. The application of factor analysis techniques to these data would be revealing The nature of the factor structure in different populations of cancer patients may vary.

The predominant causes of distress were similar to those in previous studies conducted by Holmes, and the finding that tiredness was identified as the symptom causing most distress was confirmed. The list of symptoms included in this instrument is not extensive. Subjects reported others on a number of occasions, notably hair loss and breathing difficulties. The scale was not intended to include all possible symptoms but only those symptoms identified as of most concern to the largest number of patients and this was supported in the present study. The Rotterdam Symptom Checklist (de Haes, Van Knippenberg and Neijit, 1990), which includes a more extensive list of symptoms experienced by patients undergoing cancer therapy, was not fully developed at the inception of the current study. The suitability of this instrument could usefully be explored once further studies to establish reliability and validity have been undertaken (Watson, Law, Maguire, Robertson, Greer, Bliss and Ibbotson, 1992). It would be fruitful to explore the relationship between fatigue and the presence/absence of symptoms using the Rotterdam Symptom Checklist as it included numerous symptoms/concerns added by patients to the diary.

9.3.5 Analysis

Together the visual and statistical analyses provided evidence of patterns in fatigue which cancer patients experience during chemotherapy. The heterogeneity of the sample, the

large number of variables examined and the presence of some missing data suggest that the final sample size of one hundred and nine may be too small to draw meaningful comparisons between sub-groups. In a number of the diagnostic groups (e.g. cervical cancer) small sample size inhibited detailed statistical analysis and in some cases led to the strategy of combining groups (e.g. subjects with a non-Hodgkin's and Hodgkin's lymphoma were combined as were subjects with a cholangiocarcinoma and pancreatic cancer). It also raised the probability of type II errors (non-significant findings when in fact, significant differences exist). Conducting numerous and repeated comparisons on the same data set also raised the possibility of type I errors (significant findings when in fact none exist). However, the number of spurious results were considered to have been minimised by the selection of a probability value which would reduce this possibility. In addition, and of relevance to the present study, when data are collected sequentially there is an increasing risk of rejecting the null hypothesis even when it should be verified.

Whether or not the differences found between groups during the analysis are large enough to be clinically significant might also be debated. Significance in the sense of mathematical probability is different from significance in the clinical sense. Clinical significance refers to "the meaningfulness and usefulness of the findings in the practice setting" (Oberst, 1982, p. 475). Statistically significant results may have little or no clinical significance simply because the magnitude of the difference is too small to be clinically meaningful. In selecting VASs as the principal method for estimating scores in relation to items in the diary, the researcher was influenced by a number of factors which were outlined in Chapter 5. Compared with measures that require subjects to rate the intensity of their moods, feelings or sensations on a categorical checklist, VASs do not limit subjects to a select number of possible responses, but allow them to place their responses at any point on the continuum and thus have a greater sensitivity. The individual time plots provided evidence that subjects were able to discriminate between differences in their experiences of fatigue, other symptoms and mood throughout the diary keeping period. VASs were considered particularly useful because they detected differences in the same individual, on different occasions. However, controversy remains as to their suitability when comparing scores between individuals. Thus the results should be interpreted with caution.

For instance, considering the values in table 9.1, these results were found to be significant using the Kruskal-Wallis procedure at $p<.01$, providing evidence for a significant difference in *mean fatigue scores* between the various different *types of*

Table 9.1 Results derived using the Kruskal-Wallis procedure in relation to *type of chemotherapy* and *mean fatigue score*

Type of chemotherapy	Number of observations	Median	Average rank	z value
CEOP	14	15.0	55	.8
Epirubicin and Etoposide	15	6.3	39	-1.6
CMF	5	23.9	67	1.4
Carboplatin	21	11.3	41	-1.5
Weekly 5-Fu	7	29.2	64	1.38
ECF	21	28.3	66	2.9
Weekly 5-Fu & Levamisole	10	5.4	36	-1.66
Cisplatin & 5-Fu	6	3.9	30	-1.77

H = 20.2 7 *df* $p = <.01$

chemotherapy. Differences observed between groups may be a clinically negligible difference, despite statistical significance. It is useful in these circumstances to consider the *z* value, which provides a numerical indication of the contribution each group makes to the H value. A larger value indicates greater discrepancy between the observed and expected average ranks. Although these values are not listed in the Chapters 7 and 8 they were taken into account during the selection of the results reported. This is more easily demonstrated in relation to the results obtained with the HSDS, where scores were markedly skewed towards the positive end of the scale, indicating an absence of symptom distress. Table 9.2 provides details of the results obtained in relation to *appetite* and *type of chemotherapy*. These results achieved statistical significance at $p < .01$. The clinical significance of these findings may be debated. For example, the subjects receiving Carboplatin achieved a median symptom distress score of ninety-six in relation to appetite, in comparison to eighty-one in the ECF subjects. The researcher would suggest that the observed effects in this case are large enough to be of interest. The reverse of course could also be true, some of the results may hold clinical significance in the absence of statistical significance.

Table 9.2 Results derived using the Kruskal-Wallis procedure in relation to *type of chemotherapy* and *appetite*

Type of chemotherapy	Number of observations	Median	Average rank	z value
CEOP	34	94.5	149	.95
Epirubicin and Etoposide	36	88	119	-1.5
CMF	20	99	168	1.8
Carboplatin	76	96	167	4
Weekly 5-Fu	22	80.5	110	-1.6
ECF	36	81	109	-2.3
Weekly 5-Fu & Levamisole	37	91	118.5	-1.5
Cisplatin & 5-Fu	11	79	93.1	-1.9

$H = 29.9 \quad 7\,df \quad p = <.01$

It was difficult to achieve a complete and continuous data set in this sample. Missing data, such as diaries not returned, pages not filled out, items skipped, and unclear responses inevitably lead to problems with statistical analysis. Few guidelines are available in the literature concerning techniques to handle such data. Other researchers, for example, Verbrugge (1984), used a number of approaches to complete records when skipped days occurred. These were not pursued in the current study except when subjects had been ill and were unable to complete the diary at the required time but later completed it when their health improved. Although such data became retrospective and subject to recall error they were included in the analysis.

Despite the issues mentioned above, the approaches to data collection and analysis facilitated the examination of relationships between the variables on consecutive days. This preserved the temporal relationships between the variables measured daily. These were obscured when data were aggregated. Selected components of time series analysis enabled the researcher to accurately identify the nature of the patterns which emerged from these data. The individual subject's time plots show how greatly people's trajectories of daily health may vary, and the statistical analysis revealed the demographic and medical characteristics which influence fatigue and the selected variables chosen for consideration. Chatfield (1988) advocates the search for significant sameness. It would be desirable to pursue this strategy in future studies, to determine whether the current results are repeatable. There is also a need to compare this data set to similar or related data sets. Such descriptive comparisons of different data sets will allow researchers to form a more comprehensive and empirically based model of fatigue.

CHAPTER 10

CONCLUSION

10.1 Introduction

The findings of this descriptive study are important as they supplement and expand empirical evidence on fatigue available to guide clinical care, theory development and further research. This chapter will consider some of the implications for practice, theory development and future research which emanate from this study.

10.1.1 Implications for practice

Previous clinical research has begun to provide practitioners with information about the fatigue experience which can be used in clinical practice. This study provides more data on the likely occurrence and pattern of this symptom, following the administration of chemotherapy. Most cancer patients receiving chemotherapy are likely to experience fatigue at some time. This is perceived to be distressing and to interfere with their everyday lives. Nurses could now use this information to prepare patients for impending fatigue. Coaching well in advance of the anticipated problem, coupled with the mobilisation of resources to help cope with fatigue, could prove beneficial.

Fatigue requires thorough evaluation and management, akin to those strategies adopted for the symptoms of pain and nausea. Patients often accept that fatigue will accompany their illness and treatment, frequently not mentioning it unless asked (Morris, 1982). Nurses should incorporate questions on the differing aspects of fatigue into assessment activities, including enquiries about the onset, pattern and intensity of fatigue, and the degree of distress experienced. Aggravating and alleviating factors related to fatigue and associated symptoms, such as pain and nausea, as well as changes in usual patterns of daily living, should be explored. Clarifying the nature of the symptom and its effects for the individual patient may provide the basis for further assessment and areas of focus for subsequent management.

This study revealed that the manner in which chemotherapy was administered has a definite impact on the pattern and magnitude of fatigue. This information can be of

practical benefit to patients who are preparing to undergo treatment. It would appear crucial that patients and their families are informed of the most likely period of the chemotherapy cycle when they are most at risk of experiencing fatigue and the likely trajectory of fatigue mapped out. For example, patients who receive conventional pulsed therapy might be advised to make plans that allow them to incorporate periods of rest into their daily routine for the first four to five days following bolus doses of chemotherapy. The importance of seeking help with other unrelieved symptoms should be emphasised as these are likely to contribute to the presence of fatigue. It would also be wise to communicate to patients that it is likely that they will experience an increase in fatigue around the nadir period, corresponding to the time when they are likely to be suffering from a low neutrophil count. Consideration should be given to the best ways to help patients cope in the days immediately preceding the next pulse of chemotherapy as a significant proportion of patients experienced a surge in fatigue at this time. It should also be emphasised that a number of relatively fatigue free days are likely to occur and patients could possibly be encouraged to plan activities around such days. Patients receiving weekly injections of chemotherapy, require different information. This is of key importance as this approach is becoming more common with the advent of this sort adjuvant and palliative treatment for patients with cancer of the colon.

There has been a failure in clinical practice to determine if action can be taken to prevent or ameliorate fatigue. The focus of care in cancer patients is likely to be on assisting the individual patient and their family to adapt to the fatigue state. Patients, left to their own devices, incorporate a number of strategies into their normal routine. The timing of self-care strategies in relation to the pattern of fatigue could prove crucial if they are to be of significant benefit in both the prevention and relief of fatigue. Recognition should be given by health professionals to the importance patients appear to place on maintaining a certain sense of normality in their lives as a way in which to manage the presence of fatigue.

As this study has revealed, there was considerable individual variation in the extent of fatigue reported and the amount of distress associated with this symptom. To inform the design of any individually tailored management programme, it may be useful to suggest that patients should maintain a fatigue diary for a limited period. The diary could be used to record specific fatigue levels and the relationships, if any, between specific activities and levels of fatigue. Recognising the specific pattern of fatigue could enable the individual to rearrange their daily schedule to increase activity tolerance. Furthermore, the diary could also be helpful in identifying activities that increase feelings of fatigue and evaluating methods adopted to ameliorate it. Aspects of a fatigue management programme might include:

- energy conservation techniques
- a planned exercise programme
- amelioration of concomitant symptoms
- stress reduction techniques
- psychosocial support
- nutritional counselling
- use of support networks.

Unfortunately there is little in current research to guide the selection of interventions. Until intervention studies designed to evaluate many of the interventions advocated for use with fatigued cancer patients have been conducted , we should take our lead from the patients themselves.

10.1.2 Implications for theory development

The investigation of cancer-related fatigue currently is limited by a lack of well-developed theoretical frameworks that can be used to guide clinically relevant research. Since the relationship between theory and research is held to be a close and reciprocal one, the lack of research from which theories can be generated presents a major limitation to studying fatigue. Nursing theory is a systematic method for viewing phenomena and their relationships - in this case fatigue - from a nursing perspective, in order to describe, explain, predict, or prescribe nursing care (Jacox, 1974). Theories of fatigue have the potential to clarify the relationships among potential aetiological factors, and lead to the development of effective clinical interventions.

There are a number of conceptual frameworks and theories that are currently used to organise knowledge and approaches to cancer-related fatigue which were described in the literature review. Fatigue theory has relied principally on deductive methods of theory development, from various existing theories, studies and literature reviews which have been applied to the situation of the cancer patient, particularly from the related sciences of psychology, physiology and ergonomics. This can potentially constitute a hazardous approach, in that application of theories from related sciences may occur, irrespective of the context in which they have been developed. The phenomenon of fatigue may benefit from an inductive approach to theory development, generated through nursing practice itself, based on observation of specific patient experiences, which are then generalised to other patients. Both methods of theory development hold a potential

to contribute to the identification of concepts and the establishment of relationships and the development of fatigue theory.

Concept clarification is acknowledged as an excellent strategy to use early in the theory development process. This is of particular relevance to fatigue, considering that many of the terms associated with this phenomenon have not been well defined or differentiated in the literature. This present study illustrated the benefit of asking patients themselves to reflect on the nature of fatigue and the difference, if any, they perceived between this concept and that of tiredness. Further attempts at concept clarification from the perspective of the cancer patient could lead to the development of a consistent operational definition for fatigue that can be used in research. In addition the strong correlations in this study between such symptoms as nausea, anorexia and lack of concentration suggest further energy should be invested in considering to what extent each contributes to, or is distinct from fatigue.

Piper, Lindsey and Dodd (1987) suggest that, using the strategy of theoretical substruction (a process which graphically depicts the relationships between various phenomena at different levels of abstraction), it is possible to examine the relationships that exist between the constructs of fatigue and depression in cancer patients. The present study suggests that fatigue is an independent factor, not a component of affective disturbance, as overall levels of mood disturbance were low. Studies are further required to explore more thoroughly the perception of fatigue symptoms and how these are associated with change in mood. This could be achieved using Chalder *et al.* (1993) Fatigue Scale, or alternatively, the newly developed Multidimensional Fatigue Inventory (Smets, Personal Communication, 1994) to measure fatigue, and the Hospital Anxiety and Depression Scale to assess mood disturbance. The two former instruments are short and are multidimensional in approach, all three do not contain any somatic items. This would facilitate a more complete description of the fatigue experience in cancer patients and its relation to mood states.

Empirical evidence for drawing a distinction between acute and chronic fatigue in cancer patients is lacking. However, Piper (1989) considers that the classification system most useful to nursing practice characterises fatigue as acute or chronic, principally depending on the duration of fatigue. Research concerned with fatigue in cancer patients has not generally attempted to distinguish between acute and chronic fatigue, although the prevailing view in the literature is that fatigue is chronic in nature within this population. Data from this study provide evidence that, in the majority of cancer patients receiving chemotherapy, fatigue is not a chronic problem; rather it is cyclical producing profound variation, moreover it is likely that the two states may co-exist in some

individuals. In terms of a fatigue continuum, in the literature tiredness and exhaustion are either viewed as concepts which are separate from fatigue, or are thought to lie on the same continuum but to differ in degrees of intensity. Subjects in this study mirrored this inconsistency as their opinions were divided as to whether they thought fatigue and tiredness were on the same continuum, or considered them to be different feeling states, associated with different precursors.

Clearly there is a need to develop nursing theory about fatigue. The data from this study support the adoption of a multidimensional model of fatigue as it seemed most likely that a number of causal and mediating factors were implicated, and that their relative influence varied between individuals. The relation between the patterns of fatigue and therapy is complex, and likely to be partly based on an appraisal of the meaning of the symptom for the individual patient concerned. Piper's integrated fatigue model (Piper, Lindsey and Dodd, 1987) is the most widely quoted framework available to organise the multidisciplinary perspectives, definitions and theories of fatigue in relation to clinical populations, and was used as a basis from which to plan this study. However, the results of this study present preliminary evidence that the relationships between the differing components of this framework are not likely to be straightforward and require extensive testing. Specific relationships are not predicted within the integrated fatigue model, but may be inferred. These should now be tested in factor-relating studies which may ultimately lead to the prediction of outcomes in relation to fatigue management.

Theories of self-care have been developed over the last three decades. The existence of a complex relationship between self-care and fatigue is suggested by the findings from this study, supported by the literature concerned with the role of illness and symptom interpretation and the influence of these processes on self-care. As stated in Chapter 9 interventions that are congruent with, rather then antithetical to, patient's own beliefs, are likely to be more successful.

Further development of theoretical models of fatigue is needed to provide structure for nursing research and guide revisions of theory based on the results of research. There should be a continuous communication process and exchange of ideas, observations, and research findings about fatigue amongst nurses involved in theory development, practice and research. This should be faciliated by the launch of the Fatigue Initiative In Research and Education (FIRE) under the auspices of the American Oncology Nursing Society, providing a forum for the exchange and utilisation of information about cancer-related fatigue.

10.1.3 Recommendations for future research

Although substantial progress has been made in delineating a number of aspects of the fatigue experience of people with cancer, there are a number of areas for research regarding cancer-related fatigue which are considered critical to the further development of theory, research and clinical practice. Three main areas must be addressed if understanding of fatigue is to advance in a clinically relevant manner. The discovery, development and testing of interventions effective in reducing or eliminating fatigue should form a vital strand of any future research agenda, and because the phenomenon of fatigue is complex, it may be necessary to study nursing interventions to reduce fatigue before its causes are fully understood. Investigations of the effectiveness of a supportive/educative nursing system to reduce fatigue symptom distress in cancer patients are required, which recognise the importance of individualising any intervention based on a patient's fatigue experience. Treatments need to be developed that are specific to different patient populations and care settings. How individuals monitor and react to fatigue and changes in fatigue over the course of an illness and its treatment and how this affects behaviour, self-care activity and response to interventions requires assessment.

Visual analogue scales proved a useful measurement strategy in this study. Therefore the second priority is to further develop valid and reliable ways to measure the presence and intensity of fatigue. In studying this phenomenon it would be helpful to use qualitative approaches to sensitively map and provide narrative descriptions. In-depth interviewing concerned with the fatigue experience may clarify the multiple manifestations and meanings of fatigue in cancer patients, provide information on how the perceptions of cancer populations differ from those of healthy individuals, and contribute to a consistent, research-based definition of fatigue.

The design adopted for this study proved to be successful in tracing the trajectory of fatigue and such a design should be exploited and expanded in future studies. However, the third area for study should entail further documentation of the incidence and pattern of fatigue across differing diseases, stages and treatments. Employing longitudinal, correlational and comparative designs should be pursued so that scores can be compared. The development and preliminary testing of the Multidimensional Fatigue Inventory, which was not available at the time this study was designed, is very promising (Smets, Personal Communication, 1994). How fatigue affects the perception of other symptoms such as nausea and dyspnoea should be examined. We need to develop a better understanding of the way in which potential mediating factors such as self-esteem,

social and emotional support and personal coping strategies influence the distressing effects of fatigue. Further evaluation of the best instruments to measure fatigue and differentiate fatigue from psychological states such as anxiety and depression are required.

In conclusion, the studies needed to fill the gaps in the research about fatigue in cancer patients require extensive resources. Further longitudinal studies that track fatigue throughout each phase of cancer treatment and recovery are still warranted. In such studies, large and diverse samples and fatigue measurement using multidimensional instruments could validate anecdotal evidence and support data from this study and that derived from the cross-sectional work already undertaken. Exploratory efforts in conceptualisation and measurement of the dimensions of fatigue could provide background for the expansion of what is known about fatigue measurement. Although there is a need to clarify the construct of fatigue in cancer patients, a current gap in the research is also seen in the absence of experimental studies that delineate strategies for preventing or ameliorating fatigue. Because fatigue is pervasive during all phases of the cancer illness, nurse investigators must uncover ways to intervene that dissipate this experience as a matter of some urgency. Valid intervention studies would provide the basis for improving nursing practice in the care of fatigued cancer patients.

Fatigue is a prominent problem for individuals with cancer. The fatigue state whatever its underlying mechanism, is likely to result in reduced energy and the inability to continue previously established daily activities. Minimal research has been conducted to understand the problem and its relationship to other frequently occurring phenomenon, such as pain. By better understanding the factors that contribute to fatigue, health care providers can assist individuals in developing fatigue management strategies thereby helping those with cancer, to live a fuller, more comfortable life.

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APPENDICES

Appendix A Glossary of terms

To clarify the terms used, a number of operational definitions are presented.

Fatigue
Whilst acknowledging the obvious physiological parameters of fatigue, the definition of fatigue guiding this study was limited to the subjective experience. Fatigue is characterised by subjective feelings of generalised tiredness, weariness, weakness, exhaustion and lack of energy resulting from prolonged stress that is directly or indirectly attributable to the disease process (Aistairs 1987), as indicated on a series of visual analogue scales contained in a daily diary designed for use in the present study. A number of dimensions were measured by the use of 4 visual analogue scales concerned with the extent and distress associated with fatigue, and the extent to which fatigue interferes with daily activities and activities the subject particularly enjoys.

Patients having chemotherapy
Individuals who are treated with cytotoxic drugs either singularly or in combination for the purpose of cure, control or palliation of cancer.

Symptom Distress
The patient's perception of the degree of distress from specific symptoms experienced as a result of the patient's illness or treatment (McCorkle and Young, 1978), as documented on the Holmes Symptom Distress Scale.

Self-Care Behaviour
An activity personally initiated and/or performed by the patient for the purpose of helping to ameliorate fatigue experienced as a result of the patient's illness or treatment, as recorded in a daily self-care behaviour log designed for the present study, adapted from Dodd's work.

Mood State
A subjective state of mind as measured by the patient's assessment of the extent to which a number of adjectives on the Mood Adjective Checklist describe his or her current feelings.

Appendix B Chemotherapy protocols in current use at the study site and included in the sample

Gastric and Oesophageal Cancer

The ECF protocol is used in a number of phase 2 studies for locally advanced and metastatic cancer. When utilised for squamous carcinoma of the oesophagus, resection may be considered after 3 courses, and chemotherapy is considered neo-adjuvant. Promising results have been obtained with this particular combination of drugs. Patients with this cancer have a poor prognosis, surgery can be curative, but once metastases have developed, median survival only stretches to 6 months. Adjuvant chemotherapy has not at present been demonstrated to have a place. Patients with an adenocarcinoma of the oesophagus or stomach, either locally advanced or metastatic, are randomised to the ECF versus FAMTX study.

ECF - 21 day cycle

5 - Fluorouracil	200mg/m^2	by continuous infusion daily via Hickman line
Epirubicin	50mg/m^2	3 weekly intravenous (I.V) bolus
Cisplatin	60mg/m^2	3 weekly I.V with hydration

Breast Cancer

When chemotherapy is considered in advanced breast cancer for pre and post menopausal women, a number of protocols are available

CMF - 28 day cycle

(standard)

Cyclophosphamide	100mg orally (p.o)	Days 1-14
Methotrexate	50mg I.V bolus	Day 1 and 8
5-Fluorouracil	1g I.V bolus	Day 1 and 8

or

(alternative)

Cyclophosphamide	600mg/m^2	)
Methotrexate	40mg/m^2	) all Day 1 and 8
5-Fluorouracil	600mg/m^2	)

MMM - 21 day cycle.

Methotrexate	35mg/m^2	I.V bolus	)
Mitozantrone	7mg/m^2	I.V bolus	) all Day 1
Mitomycin	7mg/m^2	I.V bolus on alternate courses	

ECF - 21 day cycle.

5-Fluorouracil	600mg/m^2	I.V bolus	)
Epirubicin	50mg/m^2	I.V bolus	) all Day 1
Cyclophosphamide	600mg/m^2	I.V bolus	)

Metastatic Adenocarcinoma of Unknown Primary

A phase 2 study given 3 weekly

5-Flourouracil 750mg/m^2 in 1L Normal Saline over 24 hours on Days 1-5

Cisplatin 60mg/m^2 IV with hydration on Day 2.

Small Cell Lung Cancer

3 course V 6 courses trial - 21 day cycle

This protocol is currently undergoing evaluation when patients present with limited or extensive disease. Combination chemotherapy induces a complete remission of between 20 and 60% in previously untreated patients. Response has been demonstrated to be similar in several series using different combinations. The optimal duration of treatment of chemotherapy for this cancer has yet to be determined , and the aim of this trial is to compare response and survival of patients treated with either 3 or 6 cycles. In those with limited stage disease who respond, thoracic irradiation is given routinely.

Epirubicin	80mg/m^2	I.V bolus day 1
Etoposide	200mg po	Day 1-4

Ovarian Cancer

A number of studies are in progress, all part of the London Gynaecological Oncology Group protocol evaluation. Patients who present with Stage II or III disease are randomised to receive high dose versus conventional carboplatin.

Conventional Chemotherapy

Carboplatin Dose (mg) = 6 (EDTA + 25), 6 cycles,every 28 days

Conventional V High Dose Therapy

Trail for stages II and III.

High Dose Carboplatin (mg) = 12 (EDTA + 25), 4 cycles,every 28 days

Conventional Dose Carboplatin (mg) = 6 (EDTA + 25), 6 cycles,every 28 days

Patients with progressive/advanced disease (trial) receive Etoposide for 7 days increasing to 10 days for 2nd course if no toxicity. The cycle repeats every 21 days. Chlorambucil is also used (non-trial) for advanced disease 10mg od for 14 days, every 28 days.

Pancreatic Cancer

The majority of patients present with locally advanced or metastatic disease which is not surgically resectable. Prognosis is poor, particularly in patients with distant metastases. Very little impact has been witnessed with the use of single agents or combination regimes. The present phase 2 studies evaluate the toxicity, response, duration and survival to this particular combination, utilising a continuous low dose of 5-Fu via an ambulatory pump.

Locally advanced disease

Randomisation to ECF ± Radiotherapy

Metastatic disease, protocol as for gastric cancer.

Cancers of the bile duct are treated with ECF.

Colorectal Cancer

Adjuvant 5-Florouracil and Levamisole is utilised for patients without metastases (follows removal of the tumor by surgery). Patients with a Dukes B carcinoma who have a poor prognosis receive this combination versus observation. Patients with a Dukes C carcinoma receive this combination versus 5-Florouracil.

5-Florouracil 450mg/m^2 I.V bolus Day 1-5, then weekly for 48 weeks commencing on Day 28. Levamisole 50mg orally TDS for 3 days, recommencing every 14 days for 1 year.

Conventional 5-Florouracil in metastatic colorectal cancer

5-Florouracil 750mg/m^2/day in IL Normal Saline over 24 hours days 1-5

Day 14 commence 5-Florouracil 750mg/m^2/day I.V bolus weekly until disease progression.

Taromustine versus 5-Florouracil in metastatic colorectal cancer (trial).

5-Florouracil 600mg/m^2 IV bolus every week until disease progression.

Continuous 5-Florouracil in metastatic colorectal cancer (trial)

A continuous infusion of 5-Florouracil (daily 300mg/m^2) is being evaluated in a randomised phase III trial versus s/c alpha 2a interferon. This regime is assessed at 8 week intervals and continued until disease advances.

Cervical Cancer

A trial which compares disease free survival and patterns of relapse in women with locally advanced disease, using neoadjuvant PM (followed by radiotherapy for all patients). It is utilised in Stage Ib and IIa bulky disease where radical radiotherapy would be the planned treatment, and StageIIb - IVa, who may have pelvic node metasteses and may have had a radical hysterectomy and pelvic lymphadenectomy.

PM given fortnightly x 3

Methotrexate 300mg/m^2 in IL Dextrose Saline + 20mmol KCI over 12 hours

T12-24 Cisplatin 60mg/m^2 in 11 Normal Saline with hydration and mannitol

Hodgkin's Disease

VEEP - 21 day cycle (trial)

Considered at 1st presentation in males where a non-sterelising therapy is preferered.

Vincristine	1.4mg/m^2	I.V day 1 and 8
Epirubicin	50mg/m^2	I.V day 1
Etoposide	200mg/m^2	p.o daily for 4 days
	or 100mg/m^2	I.V daily for 4 days
Prednisilone	60mg/m^2	p.o daily for 8 days

CHLVPP - 28 day cycle

At first presentation.

Chlorambucil	6mg/m^2/per day p.o for 14 days
Procarbazine	100mg/m^2/per day p.o for 14 days
Vinblastine	6mg/m^2 I.V day 1 and 8
Prednisilone	40mg/per day p.o for 14 days

Non Hodgkins Lymphoma

Chlorambucil or CVP/COP

Low grade lymphoma chemotherapy utilised to maximum response (part of a randomised trial).

Cyclophosphamide	750mg/m^2
Vincristine	1.4mg/m^2
Prednisilone	40mg each day p.o for 5 days

CHOP - 21 day cycle

For intermediate to high grade cases with a good prognosis CHOP or CEOP may be selected.

Cyclophosphamide	750mg/m^2	)
Adriamycin	50mg/m^2	) I.V on Day 1
Vincristine	1.4mg/m^2	)
Prednisilone	100mg p.o for 5 days	

CEOP use epirubicin rather than adriamycin (60mg/m^2)

Patients with a poor prognosis are randomised to induction chemotherapy with CHOP +/- autologous bone marrow transplant.

EPIC - every 21 days

For relapsed high grade Non Hodgkins Lymphoma

Day 1-5

Etoposide	100mg/m^2	I.V in 500mls Normal Saline over 1 hour on day 1-4
Ifosfamide (with Mesna Rescue)		I.V over 15 minutes in 100ml Normal Saline on day 1-5
Prednisoline	100mg p.o	day 1-5

Day 10

Cisplatin 60mg/m^2 IV with hydration over 4 hours.

Appendix C Patient information sheet and consent form

Patient Information Sheet

Dear Patient,

We are in the process of conducting a research study which will provide information about patients experiences during the course of chemotherapy. The main purpose of this study is to document the experience of fatigue in patients receiving chemotherapy.

The study is being carried out as part of my Doctoral Degree in Nursing. If you decide to participate in the study you will contribute by providing information on the nature of symptoms and actions taken by patients to cope with these whilst receiving chemotherapy.

Those participating in the study will be asked to complete a short diary every evening, and a number of other scales concerned with your mood and symptoms at 7 day intervals, for a period of 1 month.

If you decide to participate in the study, all information including your identity will remain confidential. A summary of the information obtained from the study will be made available to anyone of the participants who may be interested. It is not anticipated that participating in the study will cause any undue stress however if you would prefer not to answer any of the items on the questionnaires you are free to do so, and you may withdraw from the study for whatever reason at any time. If you decide not to participate in the study it will not affect your present or future care at the hospital in any way.

Please feel free to ask any questions which may be bothering you.

Thank you.

Alison Richardson
Macmillan Lecturer
Department of Nursing Studies, King's College

and

Emma Ream, Research Assistant, King's College

HEALTH AUTHORITY

DISTRICT NURSING RESEARCH/ETHICS COMMITTEE

Form of consent to participation in nursing research for use by patients/clients/volunteers.

---

1. Brief Title of Project

A Description of Fatigue In Chemotherapy Patients

The purpose of this study is to document the experience of fatigue in patients receiving chemotherapy.

The study is being carried out as part of my Doctoral Degree in Nursing. If you decide to participate in the study you will contribute by providing information of the nature of symptoms and actions taken by patients to cope with these whilst receiving chemotherapy.

Those participating in the study will be asked to complete a short diary every evening, and a number of other scales concerned with your mood and symptoms at 7 day intervals, for a period of 1 month.

If you decide to participate in the study, all information including your identity will remain confidential. A summary of the information obtained from the study will be made available to anyone of the participants who may be interested. It is not anticipated that participating in the study will cause any undue stress however if you would prefer not to answer any of the items on the questionnaires you are free to do so, and you may withdraw from the study for whatever reason at any time. If you decide not to participate in the study it will not affect your present or future care at the hospital in any way.

The study has been explained to me as described above and I have had an opportunity to ask questions. I am over the age of 18 and I voluntarily consent to participate in this study.

Signed by the person in charge of the project:

..... Date: .....

The District Nursing Research/Ethics Committee has approved the above statement. Written/Verbal consent is required for this project.

Signed by the Chairman of that Committee:

..... Date: .....

Form of consent to participation in nursing research for patients/clients/volunteers* (*delete as appropriate).

I.....of .....

....., agree to participate in the nursing research described overleaf. The nature, purpose and possible consequences of the procedures involved, summarised overleaf, have been explained to me by .... and are acceptable to me.

I understand that I am entering this project of my own free will and am free to withdraw at any time, without necessarily giving any reasons. In addition, my participation or non-participation in this project will in no way affect the care that I will receive.

Signed: (Patient/client/volunteer*).....

Witnessed by:.....

Date:.....

Appendix D Patient participation notes

Patient Participation Notes

Subject Number ☐ **Telephone Number** .....

Date ...../...../.....

1. Name .....

2. Sex .....

3. Age ☐

4. i. Diagnosis ..... 4ii. Approximate ..... Date of Diagnosis

5i. Disease Status [No Disease] [Locally advanced] [Metastatic]

5ii. Presence of Liver Metastases [Yes] [No]

6i. Intended Outcome [Non-Palliative] [Palliative]

6ii. Purpose of Chemotherapy [Neoadjuvant] [Adjuvant] [For Metastatic Disease] [For Locally Advanced Disease]

7i. Chemotherapy Protocol.....

7ii. Course of Chemotherapy ☐

7iii. Nature of administration [bolus] [continuous] [bolus and continuous]

8. Previous treatment with chemotherapy [YES] [NO]

If yes, please describe what the patient received and duration of treatment (including when treatment finished)

.....

9. Previous treatment with surgery, radiotherapy and/or endocrine therapy

[YES] [NO]

If yes, please describe what the patient received and duration of treatment (including when treatment finished)

.....

10. Expected dates of return to clinic .....

Appendix E Format of the diary used in data collection

Subject No ☐

DIARY

To help you recall each day how you have felt in general and your possible experience of fatigue and how you cope with this I have designed a diary, which is quick and easy to complete. Please could you complete the diary EACH DAY in the EVENING, starting today.

Directions:

The diary is in TWO sections. Section A should be completed every day. Section B should only be completed if you have felt fatigued that day.

To respond to each question you will be asked to place a mark on a line, place a tick in a box or write a short comment.

Please take your time and think about what each statement says and where required place a vertical mark across the horizontal line at the point which most closely resembles how you have felt that day.

For example, if you really feel quite happy today and you were asked the following question, you might answer:

How is your mood today?

(Example)

Could not feel more miserable _____ Could not feel happier

Two short additional questionnaires are included every 7 days in the diary. The instructions on how to complete these are adjacent to the questionnaires. On these days there will be no section B to complete in the diary, as some of the questions are similar.

Please try and fill in the diary every day until you return for your next course of chemotherapy. Could you please bring the completed diary with you when you return for your next course of chemotherapy, and I will collect it personally from you.

If found, please return to:-

Ms Alison Richardson or Ms Emma Ream
Department of Nursing Studies
Cornwall House Annex
Waterloo Road
London SE1 8TX

1

Date ...../...../.....

A. Please place a vertical mark across the horizontal line at the point which most closely resembles how you have felt today.

A1. To what degree today did you feel:

Calm _____ Anxious

A2. To what degree today did you feel:

Happy _____ Sad

A3. To what degree today did you feel:

Able to Concentrate _____ Unable to Concentrate

A4. How was your appetite today?

I could not face food at all _____ My appetite was normal for me

A5. How did you sleep last night?

Could not be worse _____ Slept as well as ever

A6. How much nausea did you experience today?

I felt as sick as I possibly could _____ I did not feel sick at all

Cont'd

B1. Did you feel fatigued today? Please tick the appropriate box [Yes] [No]

If the answer is **YES** please complete the items below by placing a mark through the line at the point which most closely resembles how you have felt today where this is required. If you answered **NO**, you need not complete this section.

B2. To what extent did you experience fatigue today?

No fatigue _____ A great deal of fatigue

B3. To what degree did your fatigue cause you distress today?

No distress _____ A great deal of distress

B4. To what degree did the fatigue you felt today prevent you or interfere with your ability to carry out your daily activities and chores?

Not at all _____ A great deal

B5. To what degree did the fatigue you felt today prevent you from doing the things you enjoy eg. visiting friends, going out, pursuing your hobbies?

Not at all _____ A great deal

Cont'd

B6. Please could you tick the boxes which indicate the periods of the day when you felt fatigued.

If you felt fatigued on different occassions, you can tick more than one box.

early morning	late morning	early afternoon	late afternoon	early evening	late evening

B7. Did you perform any actions which you hoped would relieve your fatigue today?

Please tick the appropriate box [Yes] [No]

If you answered **YES**, please complete the Section below:

	Action Taken	Effectiveness of Action In Relieving Fatigue (please tick a box)				Source of Idea for Action
		not relieved	partly relieved	nearly completely relieved	completely relieved	
a)	_____	1	2	3	4	_____
b)	_____	1	2	3	4	_____
c)	_____	1	2	3	4	_____
d)	_____	1	2	3	4	_____

B8. When feeling fatigued today, what do you believe contributed to or caused your fatigue?

_____

_____

B9. Did you experience any other symptoms or problems today? Please tick the appropriate box.

[YES] Please describe _____

_____

_____

[NO]

Appendix F Holmes Symptom Distress Scale

HOLMES SYMPTOM DISTRESS SCALE

Directions:

Over the page there are many different statements. Please take your time and think about what each statement says and then place a vertical mark across the horizontal line at the point which most closely resembles how you have felt today.

For example, if you really feel quite happy today and you were asked the following question, you might answer:

How is your mood today?

(Example)

Could not feel more miserable _____ Could not feel happier

Cont'd

Subject Number: ☐

Holmes Symptom Distress Scale

1. How much pain are you feeling?

Worst pain I have ever had _____ No pain

2. How much nausea are you experiencing?

I feel as sick as I possibly could _____ I do not feel sick at all

3. How is your appetite?

I cannot face food at all _____ My appetite is normal for me

4. How do you sleep?

Could not be worse _____ Sleep as well as ever

5. How mobile are you?

Completely unable to move my body _____ Normal level of physical activity for me

6. How are your bowels?

a. Diarrhoea could not be worse _____ No diarrhoea

Cont'd

b. Constipation
could not be worse _____ I am not constipated

7. How tired do you feel?

Could not feel more tired _____ I do not feel at all tired

8. Are you able to concentrate?

I cannot concentrate at all _____ My ability to concentrate is normal for me

9. How is your mood?

Could not feel more miserable _____ Could not feel happier

10. What do you feel about your appearance?

The worst it has ever been _____ My appearance has not changed

11. Is there any one symptom which is causing you severe distress?
If so, which one?_____

_____

12. Do you think the symptoms you are experiencing at present are caused by the disease or the treatment? _____

_____

_____

Appendix G Mood Adjective Checklist and key to scoring

Subject Number : ☐

MOOD ADJECTIVE CHECK LIST

Directions:

Below are a number of words which describe moods. Please respond to each item by putting a cross to indicate how much you have felt the way described today.

	Not at all	A little	Quite a bit	Extremely
Shaky				
Vigorous				
Resentful				
Nervous				
Active				
Sluggish				
Hopeless				
Lively				
Guilty				
Tired				
Unhappy				
Tense				
Full of pep				
Weary				
Worthless				
Miserable				
Worn out				
Discouraged				
Spiteful				
Depressed				
On edge				
Angry				
Furious				
Helpless				

Mood Adjective Checklist Scoring - key to mood state and corresponding adjectives

MOOD STATE	ADJECTIVE	MOOD STATE	ADJECTIVE
Depression - Dejection	Discouraged	**Vigour - Activity**	Lively
	Depressed		Vigorous
	Helpless		Active
	Hopeless		Full of Pep
	Unhappy	Range = 0-12	
	Guilty		
	Miserable	**Fatigue - Inertia**	
	Worthless		Worn Out
Range = 0-24			Tired
			Weary
			Sluggish
		Range = 0-12	
Tension - Anxiety	Shaky	**Anger - Hostility**	Furious
	Tense		Angry
	Nervous		Resentful
	On Edge		Spiteful
Range = 0-12		Range = 0-12	

Appendix H Original version of the Piper Fatigue Scale

PIPER FATIGUE SCALE

DIRECTIONS:

Each of the following questions addresses some activity or feeling which may be related to your fatigue. For each of these questions you will be asked to place a vertical mark through a horizontal line. This vertical mark should be placed through the exact spot on this line which best indicates the degree to which you are experiencing the activity or feeling. This vertical mark may be placed anywhere along the horizontal line. For example, if you really like to sleep late in the mornings, and you were asked the following question, you might answer:

1. To what degree do you usually like to sleep late in the mornings?

(Example)

Not at all _____ A great deal

Another example would include the following: If you could only sleep late in the mornings on Saturday and Sunday, and you were asked the following question, you might answer:

2. How frequently are you able to sleep in the mornings during each week, including weekends?

(Example)

Seldom _____ Often

PIPER FATIGUE SCALE T1 T2 T3 T4 T5 T6

SUBJECT NUMBER ---------- Clinical Site Code: 1 2 3 4 5

DATE ----------/----------/----------

TIME NOW ----------/----------
(Hours) (Minutes)

For each of the following questions, place a vertical mark through the line at the exact spot which best describes the fatigue you are experiencing now. If you are not now experiencing fatigue, describe what you experienced today.

1. To what degree are you experiencing fatigue now?

No fatigue _____ A great deal of fatigue

2. How severe is the fatigue which you are experiencing now?

No fatigue _____ Worst fatigue ever experienced

3. How long have you been feeling fatigued? (check one response only)

a. _____ Minutes
b. _____ Hours
c. _____ Days
d. _____ Weeks
e. _____ Months
f. _____ Other, please describe: _____

4. How would you describe the fatigue which you are feeling now?

Intermittent _____ Continuous

5. Acute _____ Chronic

6. Localized _____ Generalized
(To a specific muscle group/extremity) (Whole body is fatigued)

7. To what degree has your fatigue changed in the past week?

Decreased _____ Increased

For each of the following questions, place a vertical mark through each line at the exact spot which best indicates the degree of distress or interference you are experiencing in today's activities as a result of your fatigue.

8. To what degree is the fatigue you are feeling causing you distress?

No distress _____ A great deal of distress

9. To what degree is the fatigue you are feeling interfering with your ability to clean your house/home?

None _____ A great deal

10. To what degree is the fatigue you are feeling interfering with your ability to cook for yourself?

None _____ A great deal

11. To what degree is the fatigue you are feeling interfering with your ability to bathe or wash yourself?

None _____ A great deal

12. To what degree is the fatigue you are feeling interfering with your ability to read?

None _____ A great deal

13. To what degree is the fatigue you are feeling interfering with your ability to dress yourself?

None _____ A great deal

14. To what degree is the fatigue you are feeling interfering with your ability to complete your work or school activities?

None _____ A great deal

15. To what degree is the fatigue you are feeling interfering with your ability to visit or socialize with your friends?

None _____ A great deal

16. To what degree is the fatigue you are feeling interfering with your ability to engage in sexual activity?

None _____ A great deal

17. Overall, how much is the fatigue which you are experiencing now interfering with your ability to engage in the kind of activities you enjoy doing?

None _____ A great deal

18. How would you describe the degree of intensity or severity of the fatigue which you are experiencing now?

Mild _____ Severe

19. To what degree would you describe the fatigue which you are experiencing now as being:

Pleasant _____ Unpleasant

20. Agreeable _____ Disagreeable

21. Protective _____ Destructive

22. Positive _____ Negative

23. Normal _____ Abnormal

People feeling fatigued may experience certain feelings/sensations which indicate to them that they are fatigued. For each of the following questions, place a vertical mark through the line at the exact spot which best indicates the degree to which each feeling/sensation is being experienced by you now.

24. To what degree are you now feeling:

Refreshed _____ Exhausted

25. To what degree are you now feeling:

Strong _____ Weak

26. To what degree are you now feeling:

Awake _____ Sleepy

27. To what degree are you now feeling:

Lively _____ Listless

28. To what degree are you now feeling:

Alert _____ Drowsy

29. To what degree are you now feeling:

Refreshed _____ Tired

30. To what degree are you now feeling:

Energetic _____ Unenergetic

31. To what degree are you now feeling:

Vigorous _____ Sluggish

32. To what degree are you now feeling:

Interested _____ Bored

33. To what degree are you now feeling:

Calm _____ Nervous

34. To what degree are you now feeling:

Patient _____ Impatient

35. To what degree are you now feeling:

Motivated _____ Unmotivated

36. To what degree are you now feeling:

Happy _____ Sad

37. To what degree are you now feeling:

Relaxed _____ Tense

38. To what degree are you now feeling:

Exhilarated _____ Depressed

39. To what degree are you now feeling:

Able to Concentrate _____ Unable to Concentrate

40. To what degree are you now feeling:

Able to Remember _____ Unable to Remember

41. To what degree are you now feeling:

Able to Think Clearly _____ Unable to Think Clearly

42. Overall, what do you believe is most directly contributing to or causing the fatigue you are now experincing :

_____

_____

_____

43. Overall, when you experienced fatigue today, the best thing you found which relieved your fatigue was:

_____

_____

44. Is there anything else you would like to add that would describe your fatigue better to us? _____

_____

_____

45. Are you experiencing any other symptoms right now?
(1) NO ☐
(2) YES ☐ Please describe _____

46. Time Now: ----------/----------
(Hours) (Minutes)

Dimensions of the Piper Fatigue Scale

The Piper Fatigue Scale dimensions and respective items are as follows. The Temporal Dimension Subscale is composed of items 1, 3, 4, 5 and 7. The Severity/Intensity Dimension Subscale is composed of items 2 and 8-18. The Affective Dimension Subscale is composed of items 6, and 24-41. Item 42 measures the perceived cause of the fatigue, item 43, perceived relief measures, item 44, additional fatigue descriptors, and item 45, associated symptoms. Items 3 and 42-45 are not calculated into subscale or total fatigue scores.

Appendix I The Hospital Anxiety and Depression Scale

This questionnaire is designed to help us appreciate how you have been feeling. Read each item and place a firm tick in the box opposite the reply which comes closest to how you have been feeling in the past week.
Don't take too long over your replies: your immediate reaction to each item will probably be more accurate than a long thought-out response. Tick only one box in each section.

I feel tense or "wound up" :
(A- scale)
- Most of the time.....
- A lot of the time.....
- Time to time, Occasionally.....
- Not at all.....

I feel as if I am being slowed down :
(D-scale)
- Nearly all the time.....
- Very Often.....
- Sometimes.....
- Not at all.....

I still enjoy the things I used to enjoy :
(D-scale)
- Definitely as much.....
- Not quite so much.....
- Only a little.....
- Hardly at all.....

I get a sort of frightened feeling like 'butterflies' in the stomach :
(A-scale)
- Not at all.....
- Occasionally.....
- Quite often.....
- Very often.....

I get a sort of frightened feeling as if something awful is about to happen :
(A - scale)
- Very definitely and quite badly.....
- Yes, but not too badly.....
- A little, but it doesn't worry me....
- Not at all.....

I have lost interest in my appearance :
(D-scale)
- Definitely.....
- I don't take as much care as I should
- I may not take quite as much care...
- I take just as much care as ever.....

I can laugh and see the funny side of things :
(D-scale)
- As much as I always could.....
- Not quite so much now.....
- Definitely not so much now.....
- Not at all.....

I feel restless as if I have to be on the move :
(A-scale)
- Very much indeed.....
- Quite a lot.....
- Not very much.....
- Not at all.....

Worrying thoughts go through my mind :
(A-scale)
- A great deal of the time.....
- A lot of the time.....
- From time to time, but not too often
- Only occasionally.....

I look forward with enjoyment to things :
(D-scale)
- As much as I ever did.....
- Rather less than I used to.....
- Definitely less than I used too.....
- Hardly at all.....

I feel cheerful :
(D-scale)
- Not at all.....
- Not often.....
- Sometimes.....
- Most of the time.....

I get sudden feelings of panic :
(A-scale)
- Very often indeed.....
- Quite often.....
- Not very often.....
- Not at all.....

I can sit at ease and feel relaxed :
(A-scale)
- Definitely.....
- Usually.....
- Not often.....
- Not at all.....

I can enjoy a good book or radio or TV programme
(D-scale)
- Often.....
- Sometimes.....
- Not often.....
- Very seldom.....

Appendix J A Refinement of the Piper Fatigue Scale used in the current study

PIPER FATIGUE SCALE

DIRECTIONS:

Please complete this questionnaire. So we can find out how long it takes you to complete the questions, please fill in the time at start and time at finish where indicated. Each of the following questions addresses some activity or feeling which may be related to your fatigue. For each of these questions you will be asked to place a vertical mark through a horizontal line. This vertical mark should be placed through the spot on this line which best indicates the degree to which you have experienced the activity or feeling today. This vertical mark may be placed anywhere along the horizontal line. For example, if you really like to sleep late in the mornings, and you were asked the following question, you might answer:

1. To what degree do you usually like to sleep late in the mornings?

(Example)

Not at all _____ A great deal

Another example would include the following: If you could only sleep late in the mornings on Saturday and Sunday, and you were asked the following question, you might answer:

2. How frequently are you able to sleep in the mornings during each week, including weekends?

(Example)

Seldom _____ Often

SUBJECT NUMBER ☐

PIPER FATIGUE SCALE

For each of the following questions, place a vertical mark through the line at the spot which best describes the fatigue you are experiencing now. **If you are not now experiencing fatigue, describe what you experienced today.**

1. To what degree are you experiencing fatigue now?

No fatigue _____ A great deal of fatigue

2. How severe is the fatigue which you are experiencing now?

No fatigue _____ Worst fatigue ever experienced

3. How long have you been feeling fatigued? (check one response only)

a. _____ Minutes
b. _____ Hours
c. _____ Days
d. _____ Weeks
e. _____ Months
f. _____ Other, please describe: _____

4. How would you describe the fatigue which you are feeling now?

Occasionally _____ All the time

5. Short term _____ Long term

6. Localized _____ Generalized
(To a specific muscle group/extremity) (Whole body is fatigued)

7. To what degree has your fatigue changed in the past week?

Decreased _____ Increased

For each of the following questions, place a vertical mark through each line at the spot which best indicates the degree of distress or interference you are experiencing in today's activities as a result of your fatigue.

8. To what degree is the fatigue you are feeling causing you distress?

No distress _____ A great deal of distress

9. To what degree is the fatigue you are feeling interfering with your ability to clean your house/home?

None _____ A great deal

10. To what degree is the fatigue you are feeling interfering with your ability to cook for yourself?

None _____ A great deal

11. To what degree is the fatigue you are feeling interfering with your ability to bathe or wash yourself?

None _____ A great deal

12. To what degree is the fatigue you are feeling interfering with your ability to read?

None _____ A great deal

13. To what degree is the fatigue you are feeling interfering with your ability to dress yourself?

None _____ A great deal

14. To what degree is the fatigue you are feeling interfering with your ability to complete your work or school activities?

None _____ A great deal

15. To what degree is the fatigue you are feeling interfering with your ability to visit or socialize with your friends?

None _____ A great deal

16. To what degree is the fatigue you are feeling interfering with your ability to engage in sexual activity?

None _____ A great deal

17. Overall, how much is the fatigue which you are experiencing now interfering with your ability to engage in the kind of activities you enjoy doing?

None _____ A great deal

18. How would you describe the degree of intensity or severity of the fatigue which you are experiencing now?

Mild _____ Severe

19. To what degree would you describe the fatigue which you are experiencing now as being:

Pleasant _____ Unpleasant
20. Agreeable _____ Disagreeable
21. Beneficial _____ Harmful
22. Positive _____ Negative
23. Normal _____ Abnormal

People feeling fatigued may experience certain feelings/sensations which indicate to them that they are fatigued. For each of the following questions, place a vertical mark through the line at the spot which best indicates the degree to which each feeling/sensation is being experienced by you now.

24. To what degree are you now feeling:

Refreshed _____ Exhausted

25. To what degree are you now feeling:

Strong _____ Weak

26. To what degree are you now feeling:

Awake _____ Sleepy

27. To what degree are you now feeling:

Lively _____ Listless

28. To what degree are you now feeling:

Alert _____ Drowsy

29. To what degree are you now feeling:

Refreshed _____ Tired

30. To what degree are you now feeling:

Energetic _____ Unenergetic

31. To what degree are you now feeling:

Vigorous _____ Sluggish

32. To what degree are you now feeling:

Interested _____ Bored

33. To what degree are you now feeling:

Calm _____ Nervous

34. To what degree are you now feeling:

Patient _____ Impatient

35. To what degree are you now feeling:

Motivated _____ Unmotivated

36. To what degree are you now feeling:

Relaxed _____ Tense

37. To what degree are you now feeling:

Happy _____ Sad

38. To what degree are you now feeling:

Exhilarated _____ Depressed

39. To what degree are you now feeling:

Able to Concentrate _____ Unable to Concentrate

40. To what degree are you now feeling:

Able to Remember _____ Unable to Remember

41. To what degree are you now feeling:

Able to Think Clearly _____ Unable to Think Clearly

42. Overall, what do you believe is most directly contributing to or causing the fatigue you are now experiencing? _____

_____

_____

_____

43. Overall, when you experienced fatigue today, the best thing you found which relieved your fatigue was: _____

_____

_____

_____

44. Is there anything else you would like to add that would describe your fatigue better to me? _____

_____

_____

_____

45. Are you experiencing any other symptoms right now?

(1) NO ☐
(2) YES ☐ Please describe _____

_____

_____

_____

Scoring of the Piper Fatigue Scale

1. Measure each visual analogue scale (0-100mm) and code fixed response and open ended items (3, 42, 43, 44, 45)

2. Calculate subscale scores by summing the scores on all the items within a particular subscale and divide by the number of items within subscale. This gives a Mean Subscale Score.

   Temporal subscale Questions 1, 4, 5 & 7 (4 items)
   Severity/Intensity Subscale Questions 2, 8, 9 & 10 - 18 (12 items)
   Affective Subscale Questions 19-23 (5 items)
   Sensory Subscale Questions 6, 24-41 (19 items)

If 75% or more of each Subscale is answered, may use mean item substitution to calculate missing items in order to determine the subscale score ie.

Temporal Subscale	3 out of 4 items
Severity/Intensity Subscale	9 out of 12 items
Affective Subscale	4 out of 5 items
Sensory Subscale	15 out of 19 items

3. Total Fatigue Score is calculated by adding the four mean subscale scores together and dividing by 4.

Mean subscale scores rather than actual subscale scores are used as some dimensions have a greater number of items and so would be unfairly weighted if used actual subscale scores.

Appendix K Preliminary interview

Subject Number ☐

Preliminary Interview

To be initiated following an explanation of the purpose of the study and consent to participate has been gained. The questions below are listed to be used a prompts by the researcher.

An explanation will be given by the researcher suggesting they would like to have a short chat with the patient, so that the researcher can gain an insight into the life style of the patient and consequently understand the information from the diary more fully.

A. Health Status

1. I am aware of your present illness but are there any other enduring health problems which you have and affect your everyday life?

B. Ability to manage at home

2. Who lives at home with you?
3. Are you able to manage independently at home?

   What kind of help and support do you get from your family and friends, around the house?
4. Do you have any services provided by the social service department?
5. Do you have any particular demands on your time and energy?

C. Employment

6. Do you usually work ? (maybe housewife, retired, long-term sick leave)
7. Are you currently still working? (part-time, full-time or intermittent)

D. Fatigue

8. In your opinion are tiredness and fatigue the same thing, or do they represent different things to you?

9. Have you found fatigue to be a problem recently?

10. If so, is there anything you could put it down to or link it with:-

- the illness itself
- the treatment
- change in sleep
- other symptoms
- depression/mood
- demands of home and work

11. Do you expect this to be a problem now you are starting chemotherapy /with this course of chemotherapy?

The questions below should not be asked if the patient has no current experience of fatigue.

12. Do you feel the fatigue you experience now is the same or different than any fatigue you experienced before you were ill / before you commenced chemotherapy?

13. Do you feel the fatigue you experience presently to be abnormal/unusual or normal/usual?

14. Does your present fatigue occur everyday or just occasionally?

15. Is your fatigue a problem for all or most of the day or just at certain times?

Conclude by thanking the person for giving you the information and proceed to reinforce instructions for participating in the study and ascertaining if they are willing to be telephoned at home.

Appendix L Parting interview

Subject Number ☐

Parting Interview

After thanking the patient for their time and effort whilst filling the diary in, explain that you would like a short chat to find out how they found the completion of the diary and how the last month has been.

A. Diary

1. Was the diary a) difficult b) time consuming c) a lot of effort d) repetitive to complete?

2. Did you manage to fill it in every evening or were there times when you filled it in at another time?

B. Health Status

1. Has your health status remained constant throughout the month or have you suffered infections, anaemia ..... other problems since we last met a month ago?

C. Ability to manage at home

1. Are you still managing as much around the house as you were at the beginning of the study. If not how has this changed?

2. Are the same people still helping you, or is there anybody different involved?

D. Employment

1. Have you continued to work during the past month or has your pattern of employment changed?

E. **Fatigue**

1. Do you feel that your fatigue has significantly altered during this latest course of chemotherapy? If so, why do you think this was the case?

2. Did you find that anything significantly helped you throughout the month when you were feeling fatigued?

3. Do you think there is any way in which the nurses and doctors in the hospital could help you cope better with your fatigue?

One other instrument helps to describe peoples fatigue and is very helpful to us. Would you feel up to filling in one last brief questionnaire?

Appendix M An example of a coding sheet developed for the study

Coding Frame - Patient Participation Variables

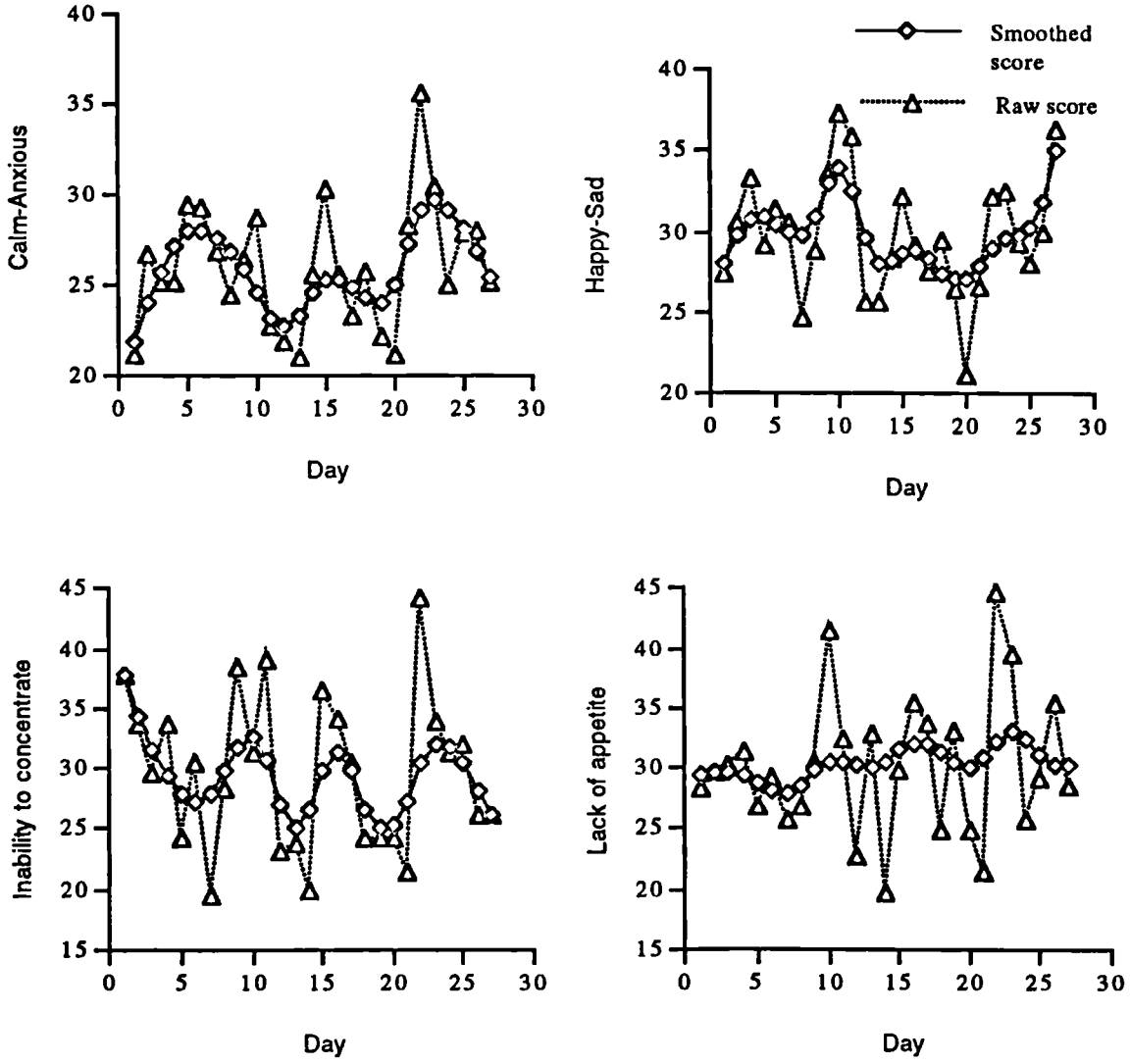
Worksheet Column	WORKSHEET NAME : DEMOGRAPHIC . MTW		
C1	1.	Patient Number: ☐	
C2	2.	Sex: Male (1) Female (2)	
C3	3.	Age: Insert Value	
C4	4. i.	Diagnosis:	Small Cell Lung (1) Breast (2) NH Lymphoma (3) H Lymphoma (4) Cervix (5) Ovary (6) Colon/Rectal (7) Stomach (8) Pancreas (9) Unknown primary (10) Bile duct (11)
C5	4.ii.	Date of Diagnosis	(1) 0-3 months previously (2) 4-6 months previously (3) 7-12 months previously (4) over 12 months ago
C6	5. i.	Disease status prior to chemotherapy	(1) No disease (2) Locally Advanced (3) Metastatic
C7	5.ii.	Presence or absence of liver metastases:	(1) Negative (2) Positive
C8	6. i.	Intended Outcome:	(1) Non-palliative (2) Palliative
C9	6.ii.	Purpose of Chemotherapy:	(1) Neo adjuvant (2) Adjuvant (3) For metastatic disease (4) For locally advanced when not neo adjuvant

C10	7. i.	Chemotherapy Protocol:	(1) CEOP (2) EPI (+/- VP16) (3) CMF (4) CHLVPP (5) Carboplat (6) High dose carboplat (7) MM/MMM (8) 5-Fu Bolus weekly (9) ECF (10) 5-Fu + levamisole (11) Cisplatin + 5-Fu (12) EPIC (13) PMB
C11	7.ii.	Course:	(1) (2) (3) (4) (5) (6) (*) for weekly 5-Fu
C12	7.iii.	Nature of Administration:	(1) Bolus (2) Bolus & Continuous (3) Intermittent Bolus
C13	8. i.	Previous treatment with chemotherapy:	(1) YES (2) NO
C14	8.11.	When Complete: Not applicable	(1)) (2)) (3)) (4)) (5)))
C15	8.iii.	Type: Not applicable	(1)) (2)) (3)) (4)) (5)) (6)) (7)) (8)) (20)) Code as above
C16	9. i.	Previous treatment with surgery, radiotherapy and/or endocrine therapy:	(1) YES (2) NO
C17	9.ii.	Surgery:	(1) YES (2) NO

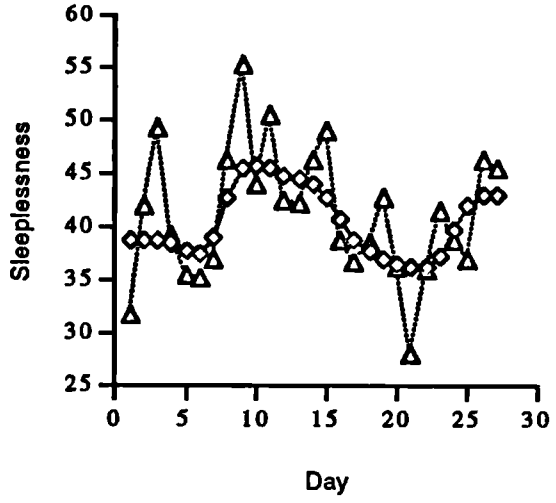
C18	9.iii.	When:	(1)	)
			(2)	)
			(3)	)
			(4)	)Code as above
		Not applicable	(5)	
C19	9. iv.	Radiotherapy:	(1)	YES
			(2)	NO
C20	9. v.	When Completed:	(1)	)
			(2)	)
			(3)	)
			(4)	) Code as above
			(5)	)
C21	9. vi	Endocrine:	(1)	YES
			(2)	NO
C22	9.vii.	When Completed:	(1)	)
			(2)	)
			(3)	)
			(4)	) Code as above
			(5)	)
		Continuous	(6)	

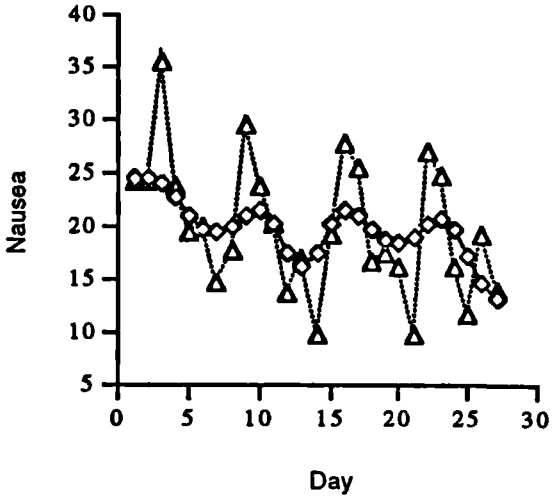
Appendix N Time plots of raw and "smoothed" daily diary items of subjects receiving different types of chemotherapy

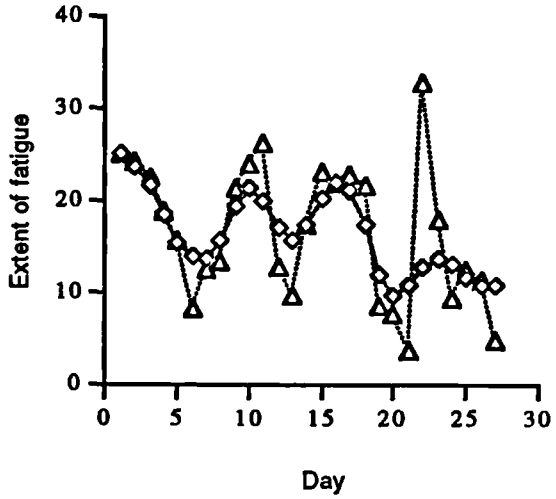
5-Fu and Levamisole

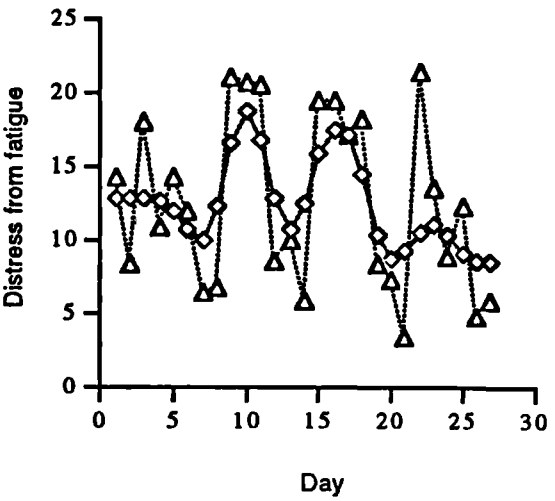


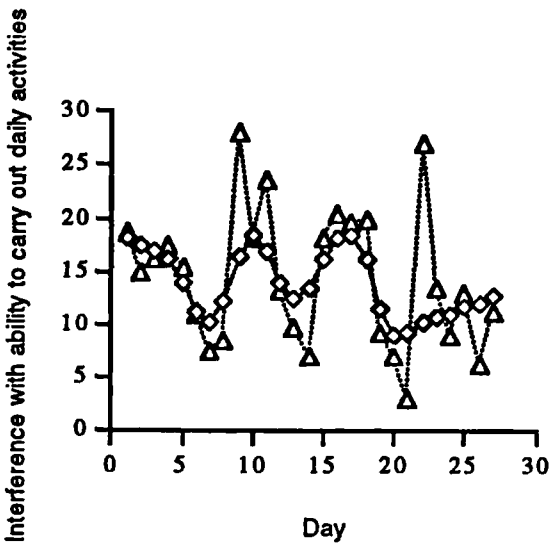
5-Fu and Levamisole (Cont'd)

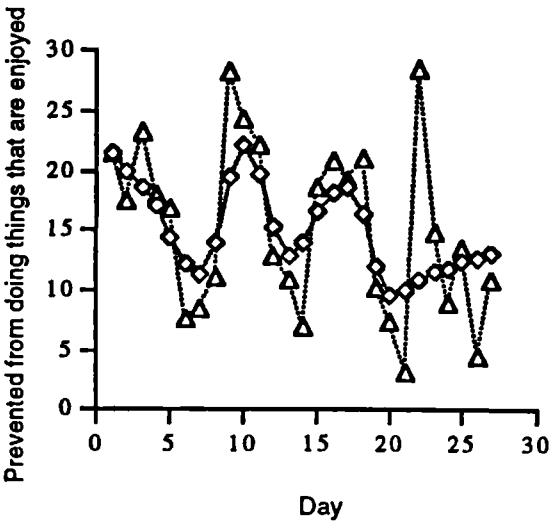




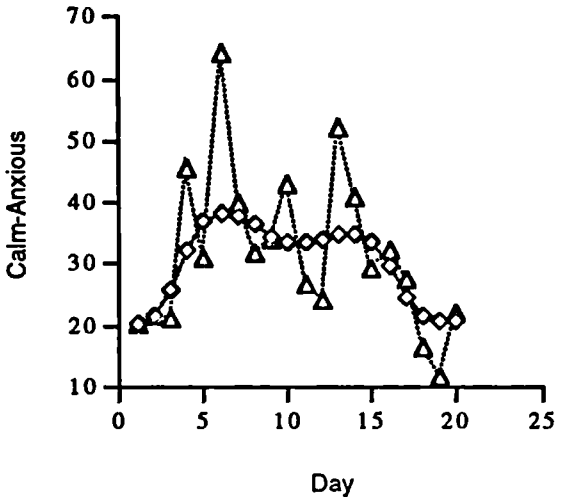


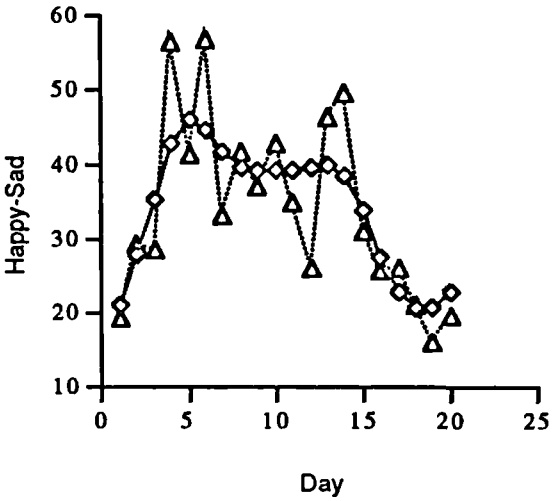


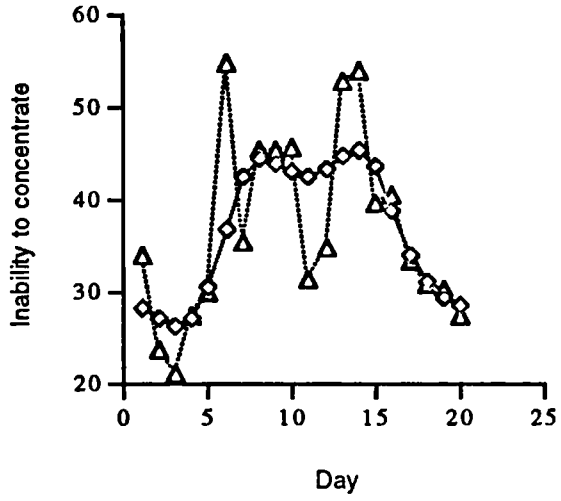


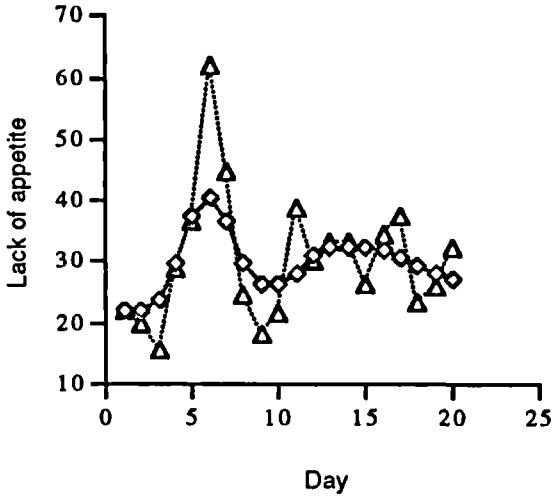


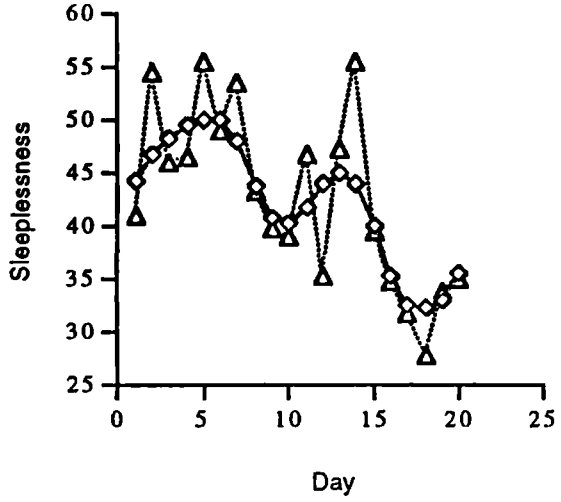
5-Fu and Cisplatin

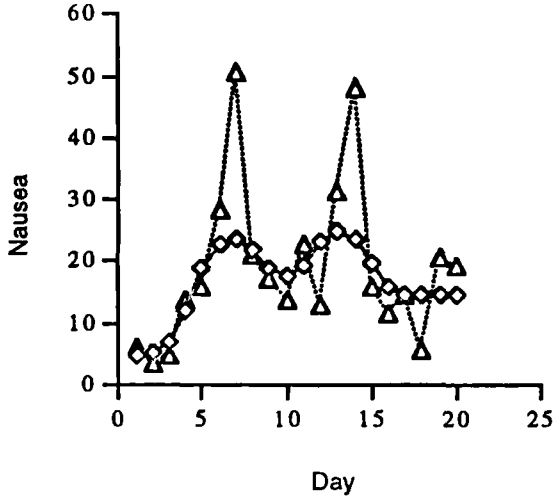












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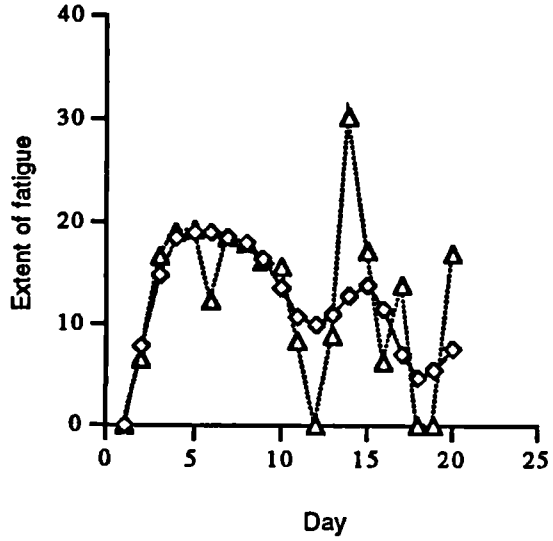
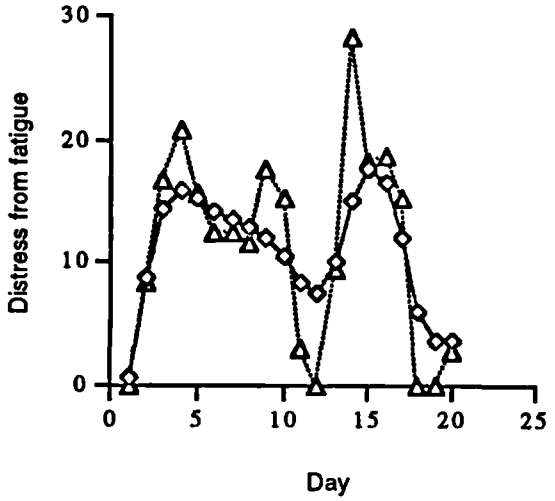
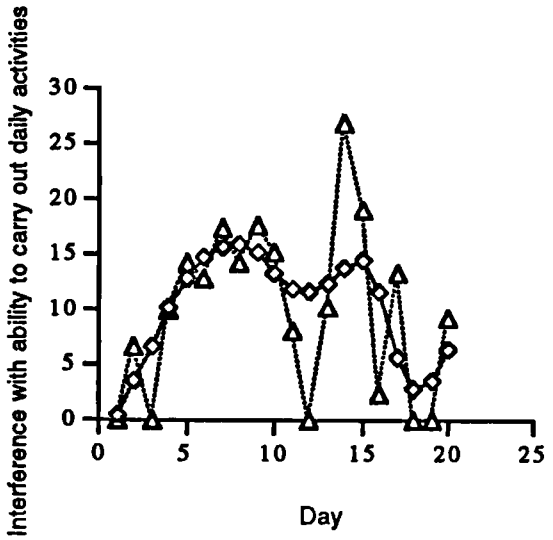
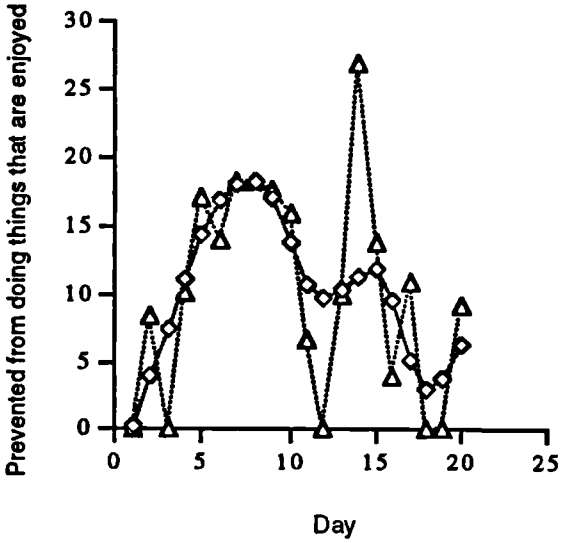
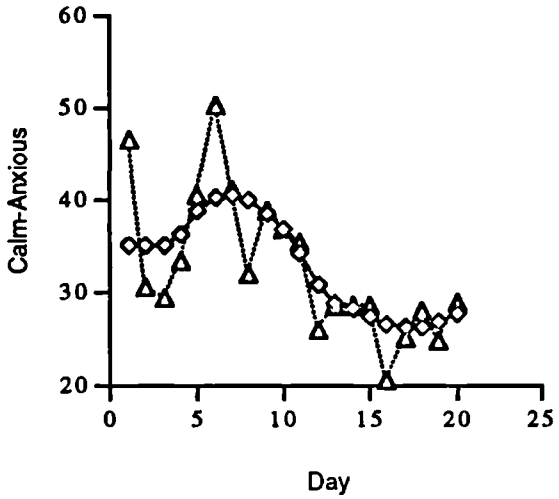


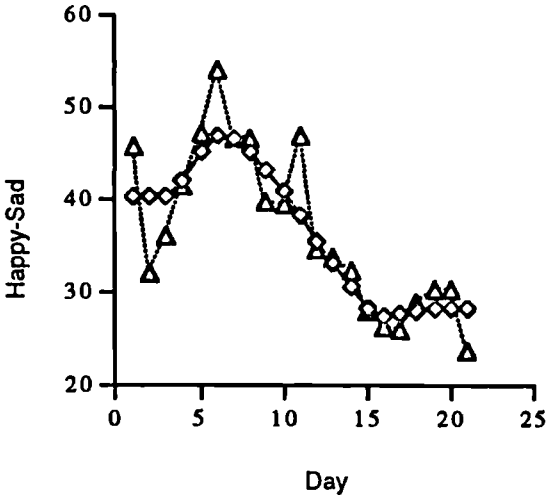


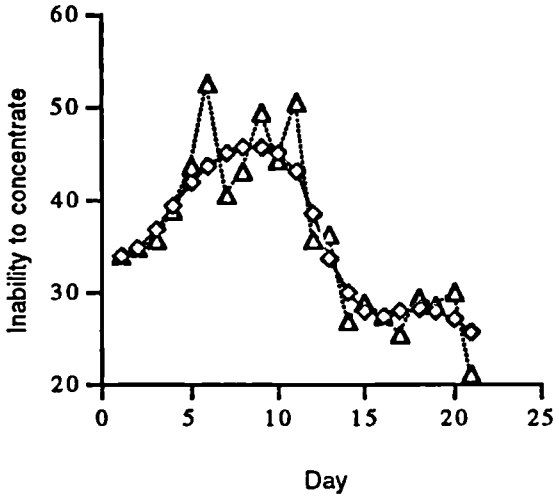


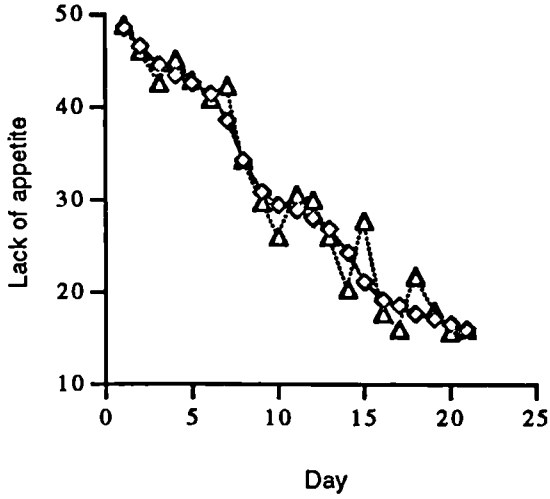


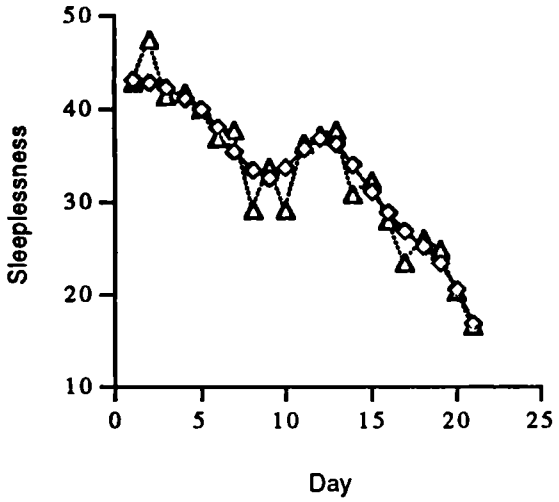
ECF

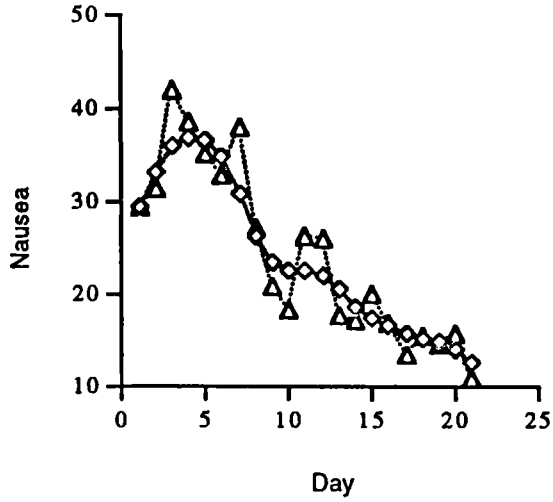

Calm-Anxious
60
50
40
30
20
0
5
10
15
20
25
Day


Happy-Sad
60
50
40
30
20
0
5
10
15
20
25
Day

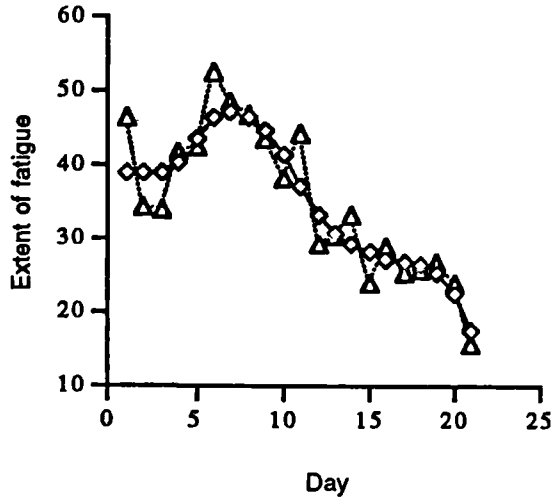

Inability to concentrate
60
50
40
30
20
0
5
10
15
20
25
Day

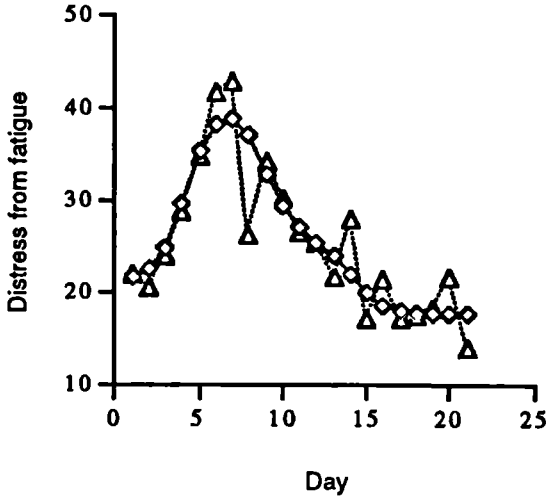

Lack of appetite
50
40
30
20
10
0
5
10
15
20
25
Day

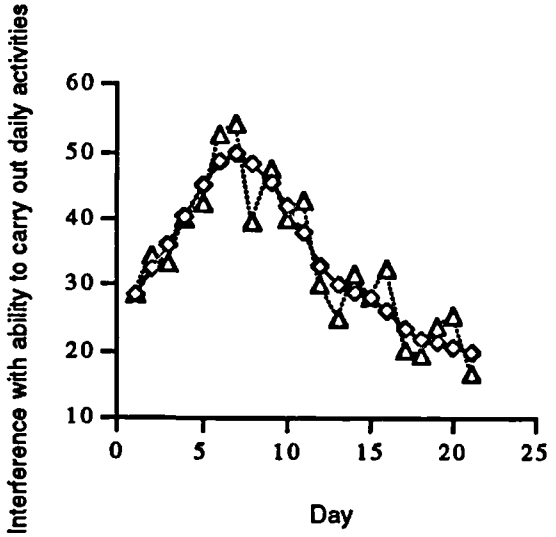

Sleeplessness
50
40
30
20
10
0
5
10
15
20
25
Day

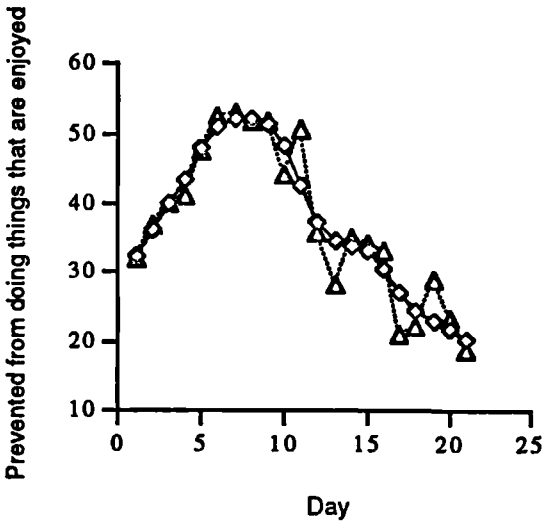

Nausea
50
40
30
20
10
0
5
10
15
20
25
Day

ECF (Cont'd)

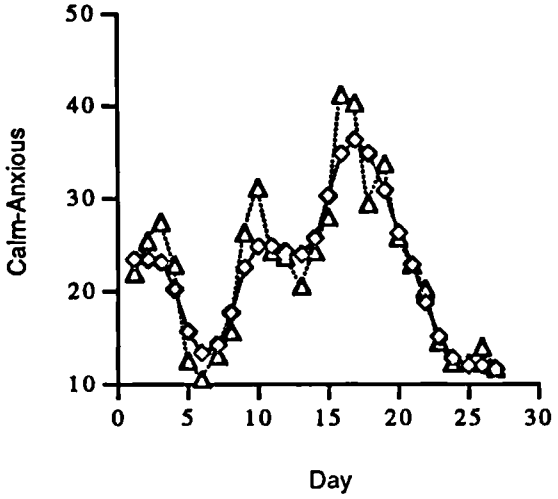

Extent of fatigue
60
50
40
30
20
10
0
5
10
15
20
25
Day

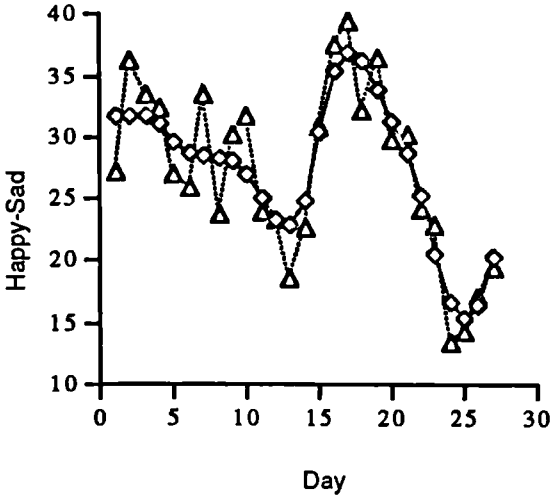

Distress from fatigue
50
40
30
20
10
0
5
10
15
20
25
Day

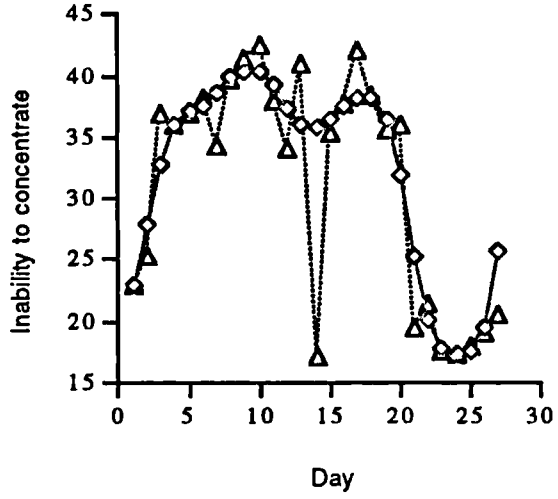

Interference with ability to carry out daily activities
60
50
40
30
20
10
0
5
10
15
20
25
Day

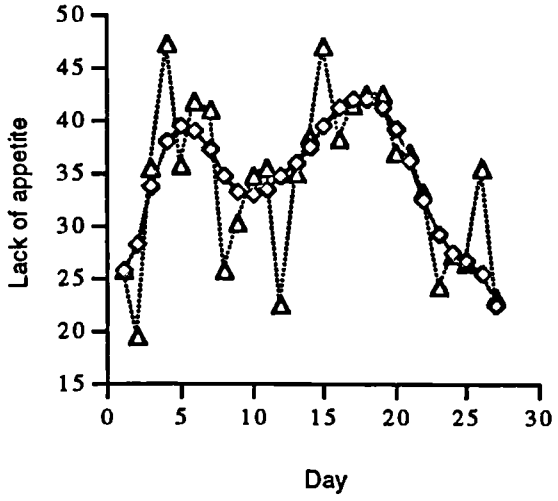

Prevented from doing things that are enjoyed
60
50
40
30
20
10
0
5
10
15
20
25
Day

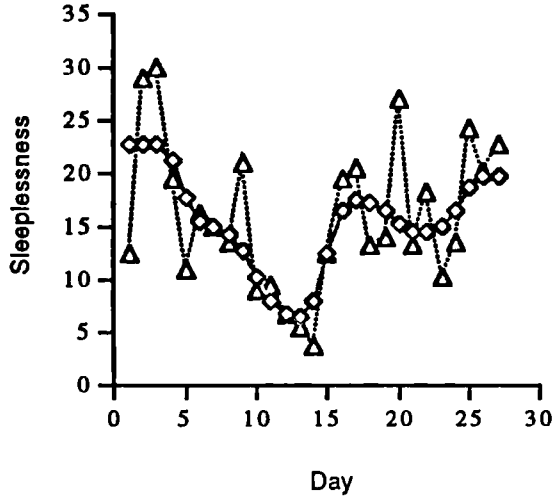
5-Fu weekly

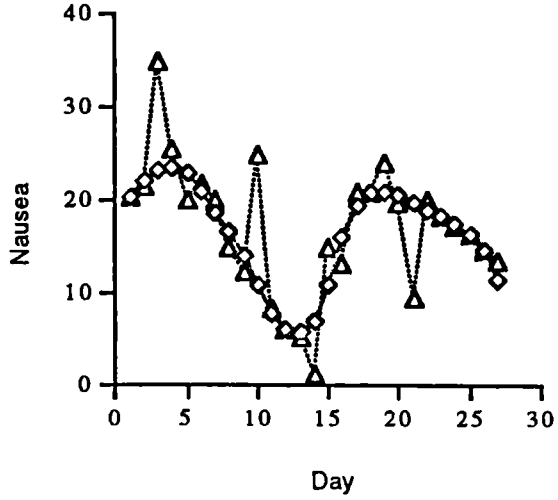

Calm-Anxious
50
40
30
20
10
0 5 10 15 20 25 30
Day


Happy-Sad
40
35
30
25
20
15
10
0 5 10 15 20 25 30
Day

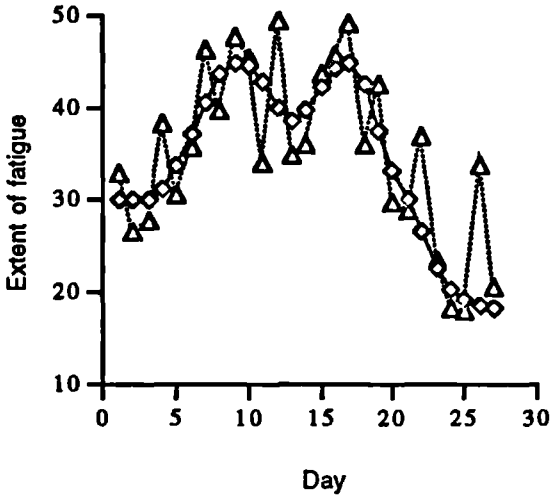

Inability to concentrate
45
40
35
30
25
20
15
0 5 10 15 20 25 30
Day

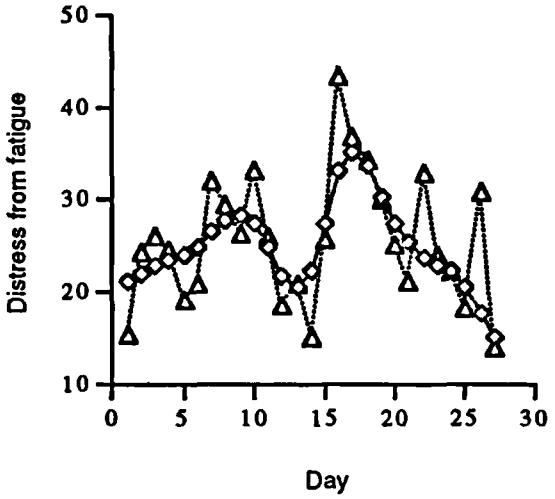

Lack of appetite
50
45
40
35
30
25
20
15
0 5 10 15 20 25 30
Day

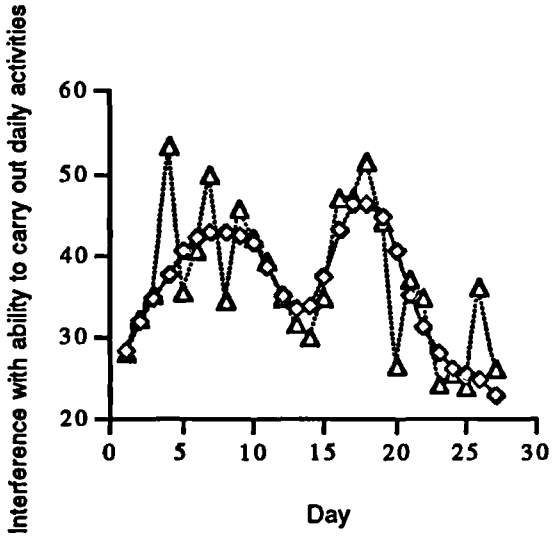

Sleeplessness
35
30
25
20
15
10
5
0
0 5 10 15 20 25 30
Day

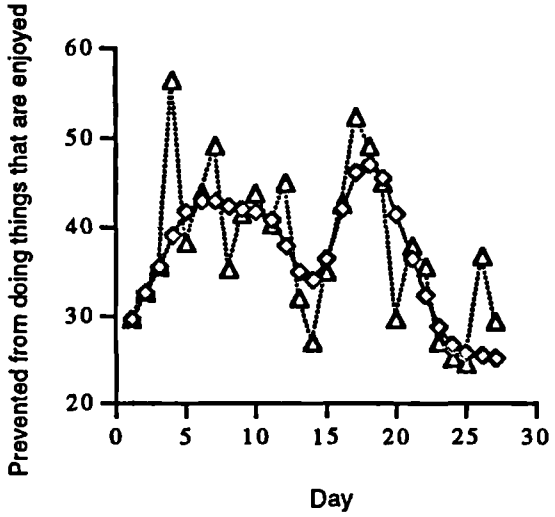

Nausea
40
30
20
10
0
0 5 10 15 20 25 30
Day

5-Fu weekly (Cont'd)

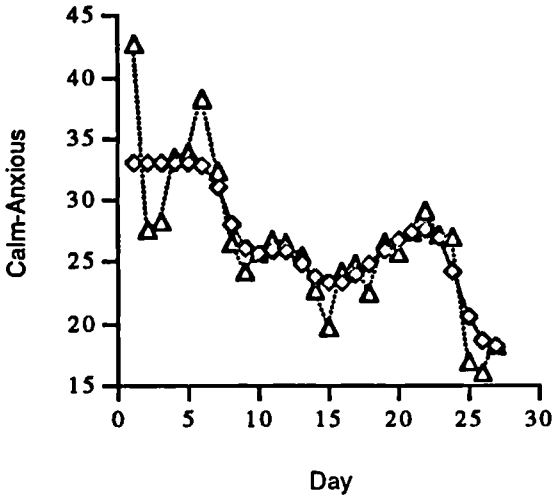


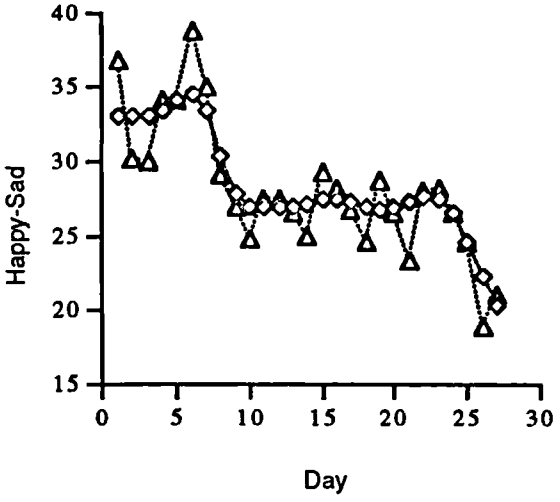


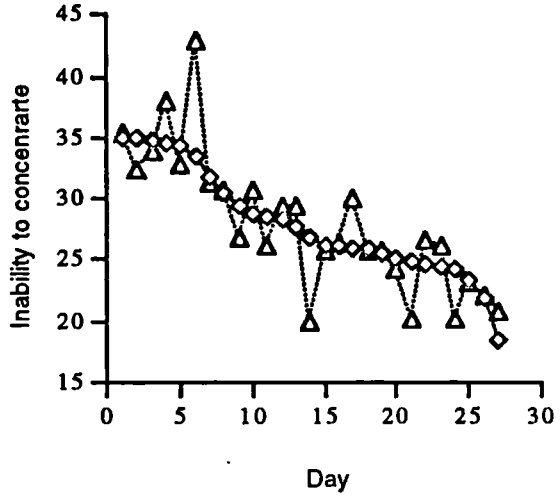


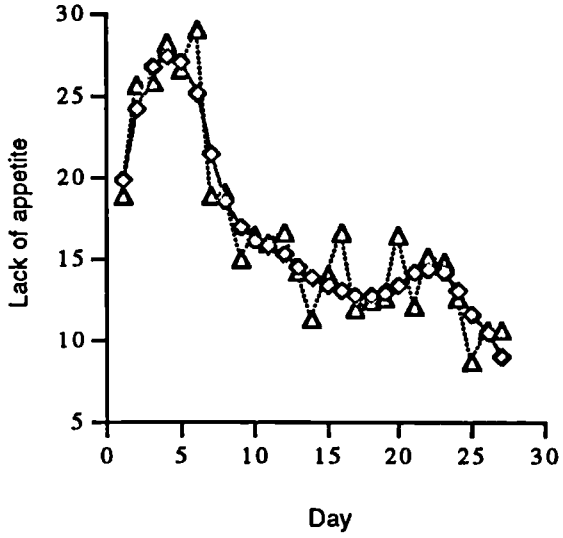


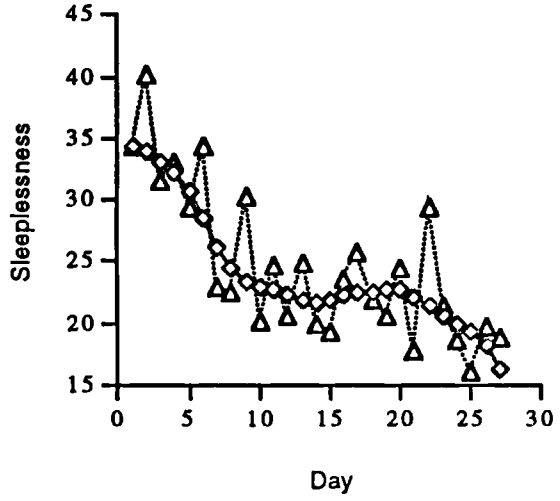
Carboplatin

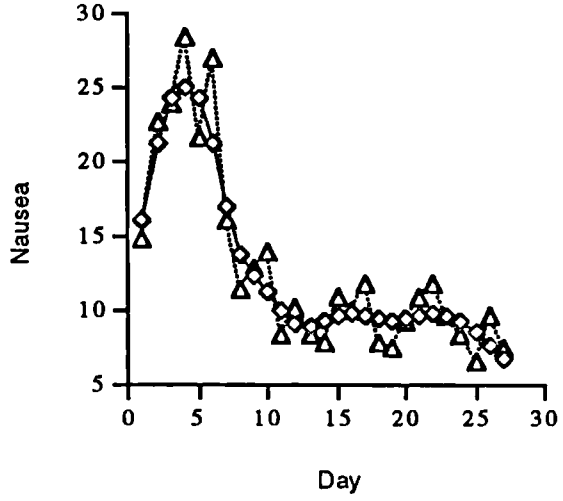












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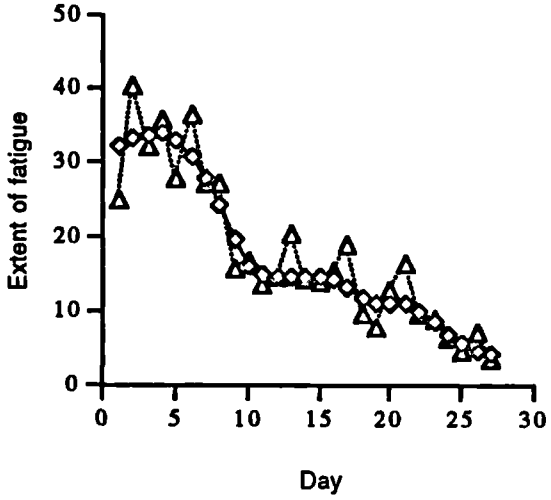
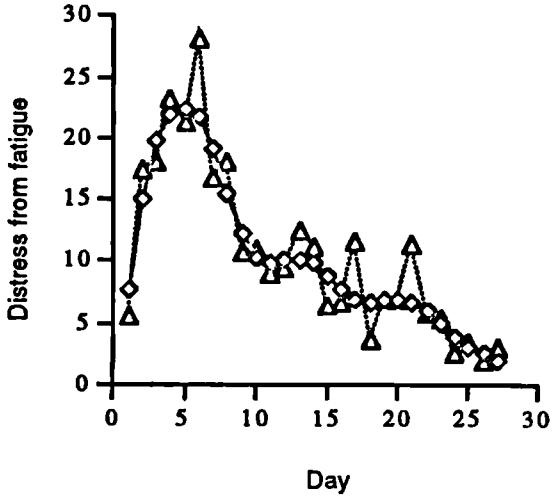
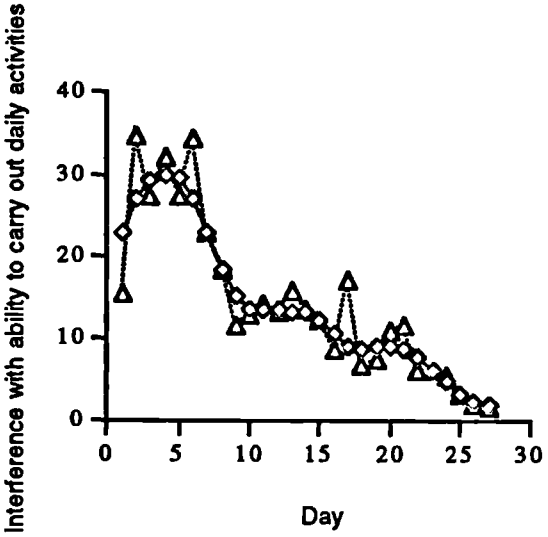
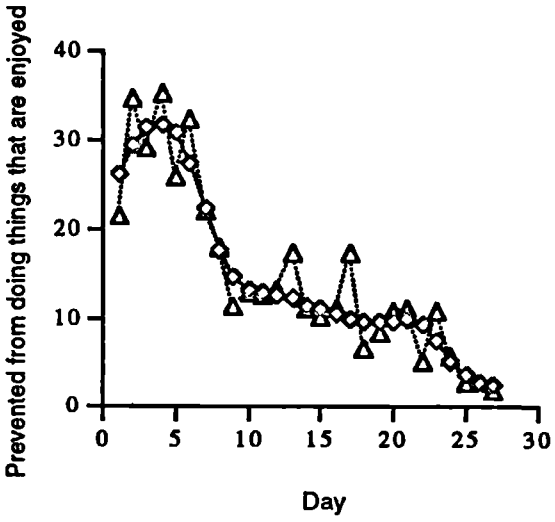
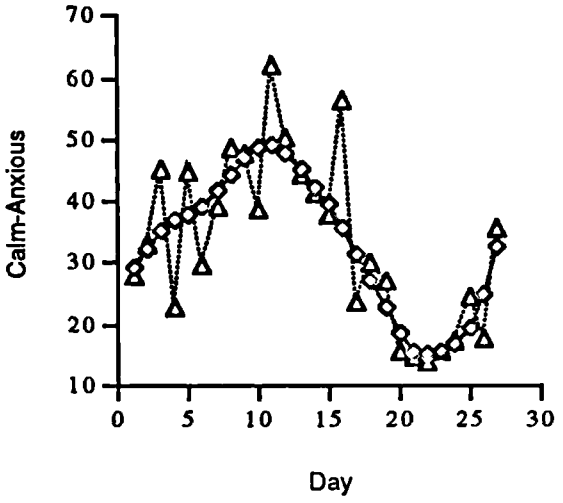


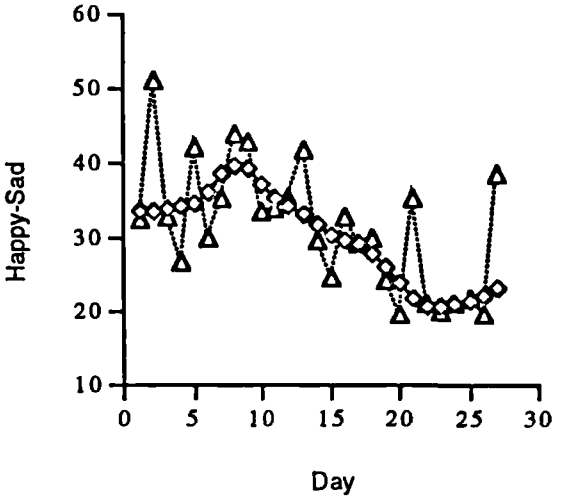


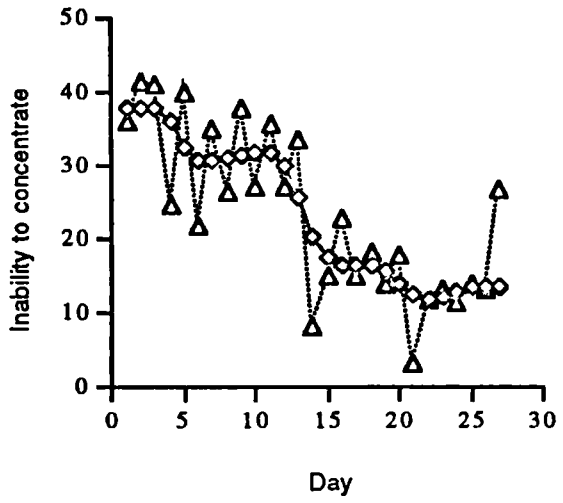


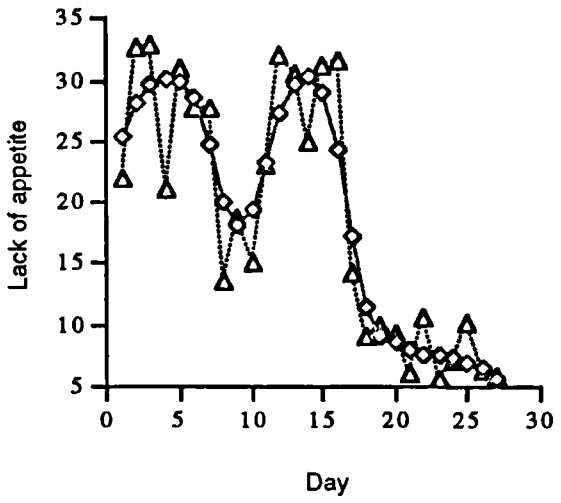


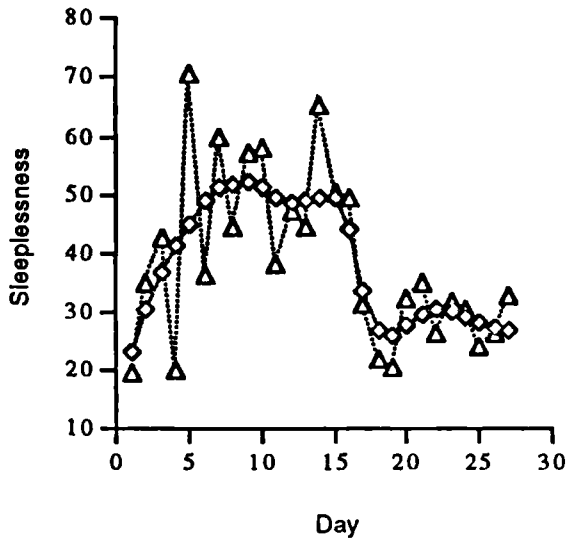
CMF

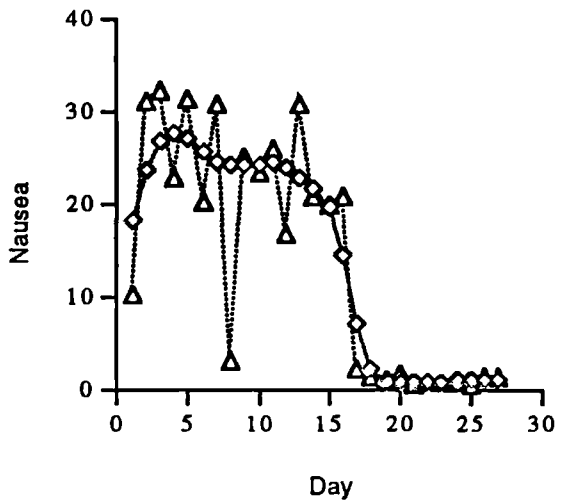

Calm-Anxious
70
60
50
40
30
20
10
0 5 10 15 20 25 30
Day


Happy-Sad
60
50
40
30
20
10
0 5 10 15 20 25 30
Day

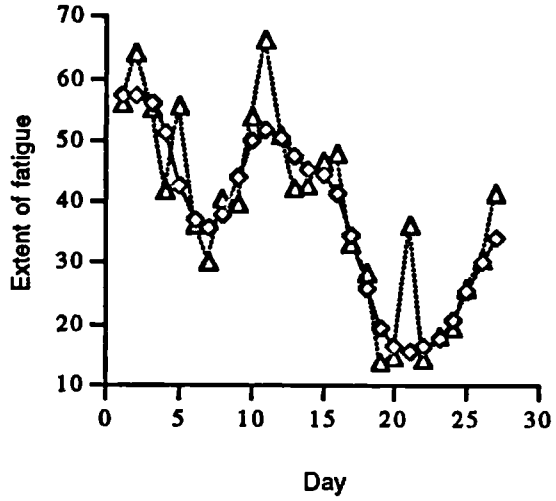

Inability to concentrate
50
40
30
20
10
0
0 5 10 15 20 25 30
Day

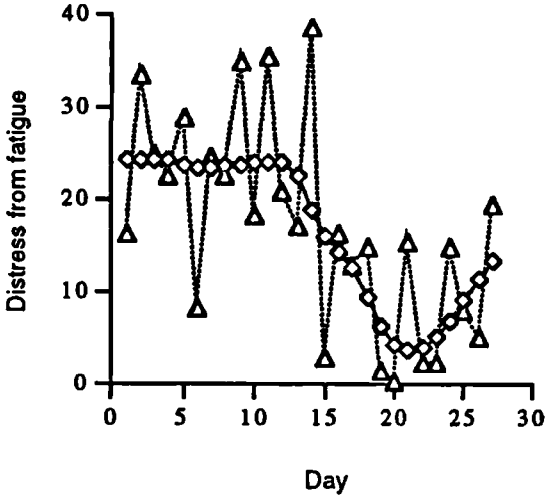

Lack of appetite
35
30
25
20
15
10
5
0 5 10 15 20 25 30
Day

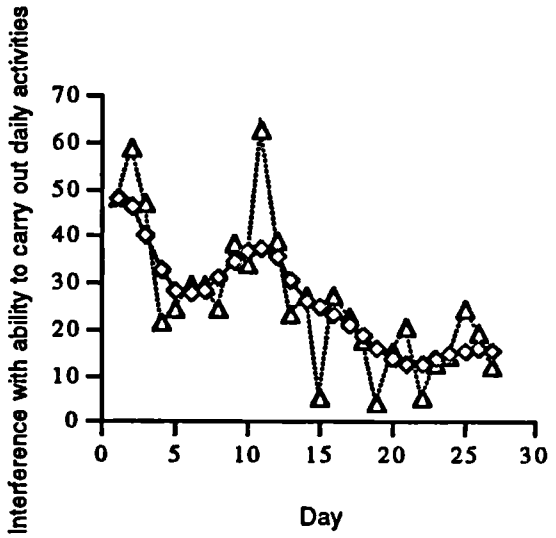

Sleeplessness
80
70
60
50
40
30
20
10
0 5 10 15 20 25 30
Day

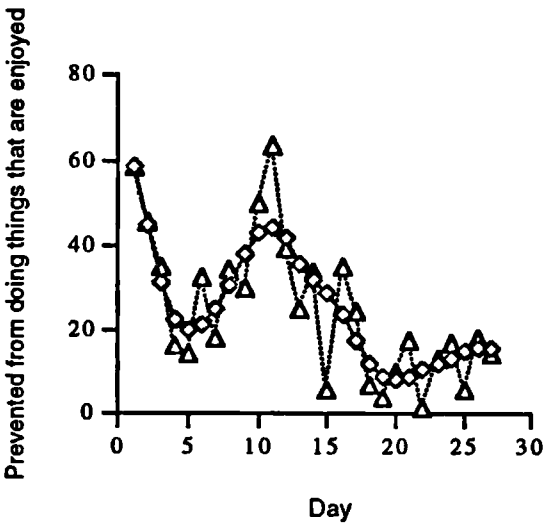

Nausea
40
30
20
10
0
0 5 10 15 20 25 30
Day

CMF (Cont'd)

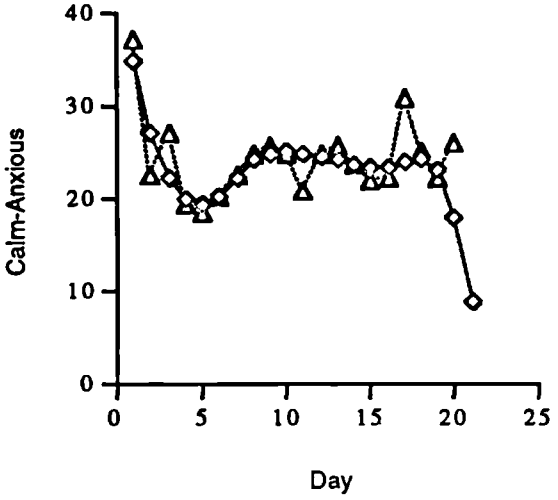

Extent of fatigue
70
60
50
40
30
20
10
0
5
10
15
20
25
30
Day

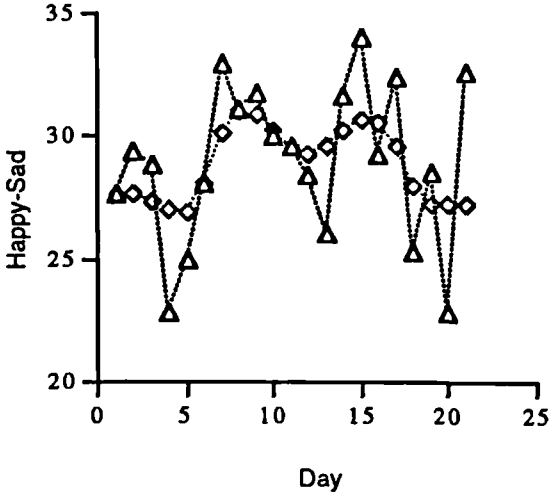

Distress from fatigue
40
30
20
10
0
0
5
10
15
20
25
30
Day

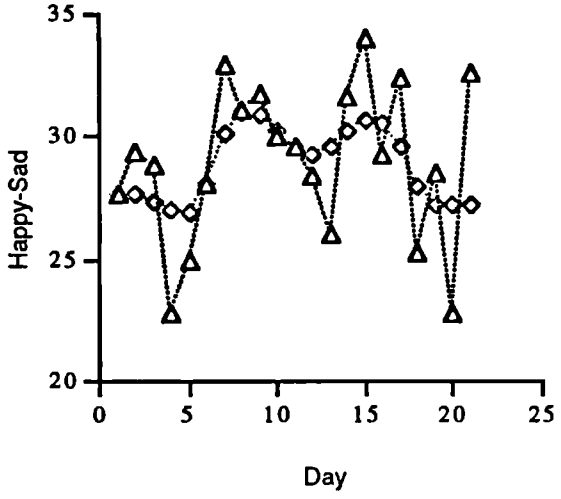

Interference with ability to carry out daily activities
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30
Day

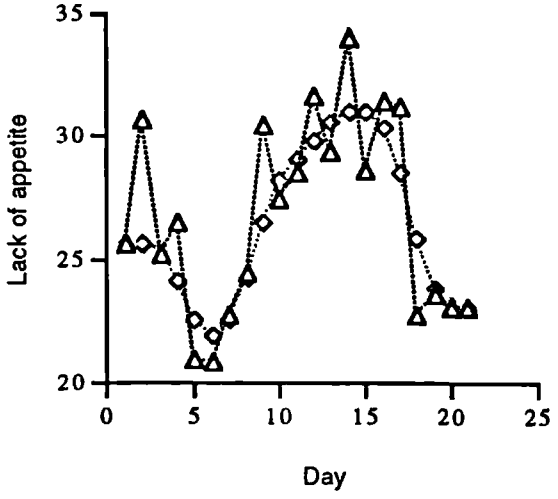

Prevented from doing things that are enjoyed
80
60
40
20
0
0
5
10
15
20
25
30
Day

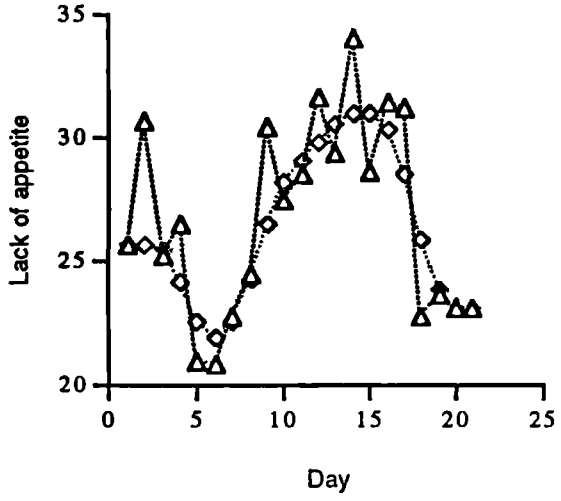
Epirubicin and Etoposide

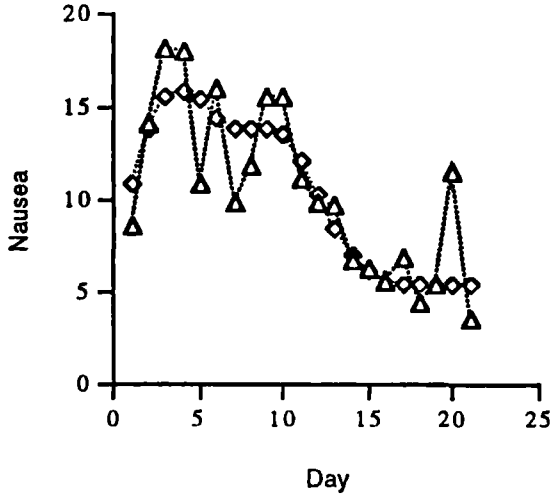




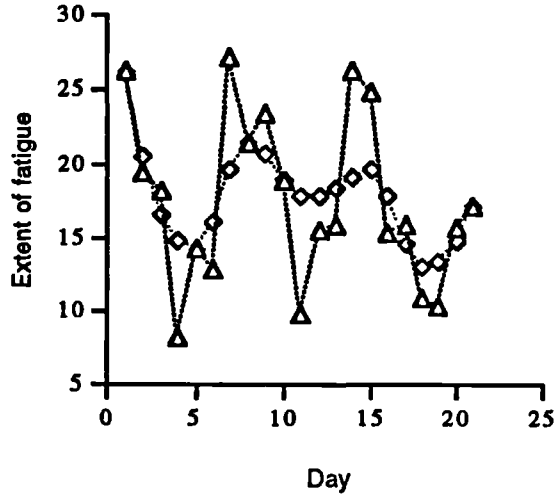


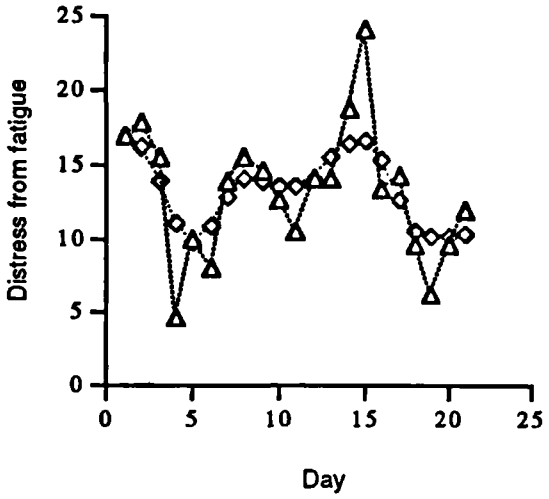


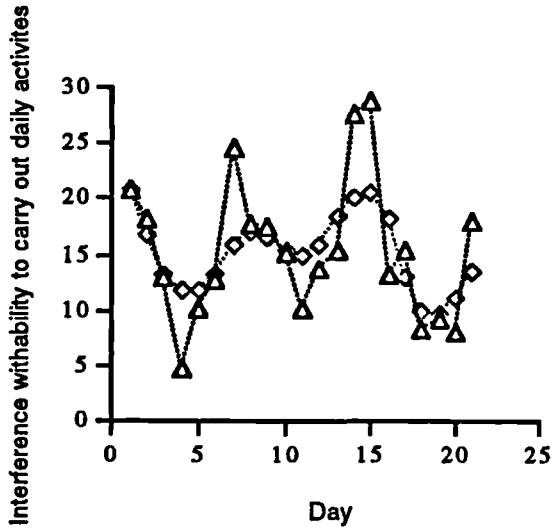


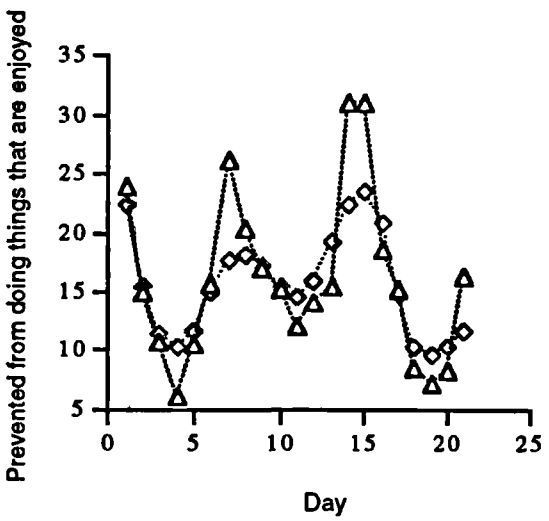


Epirubicin and Etoposide (Cont'd)

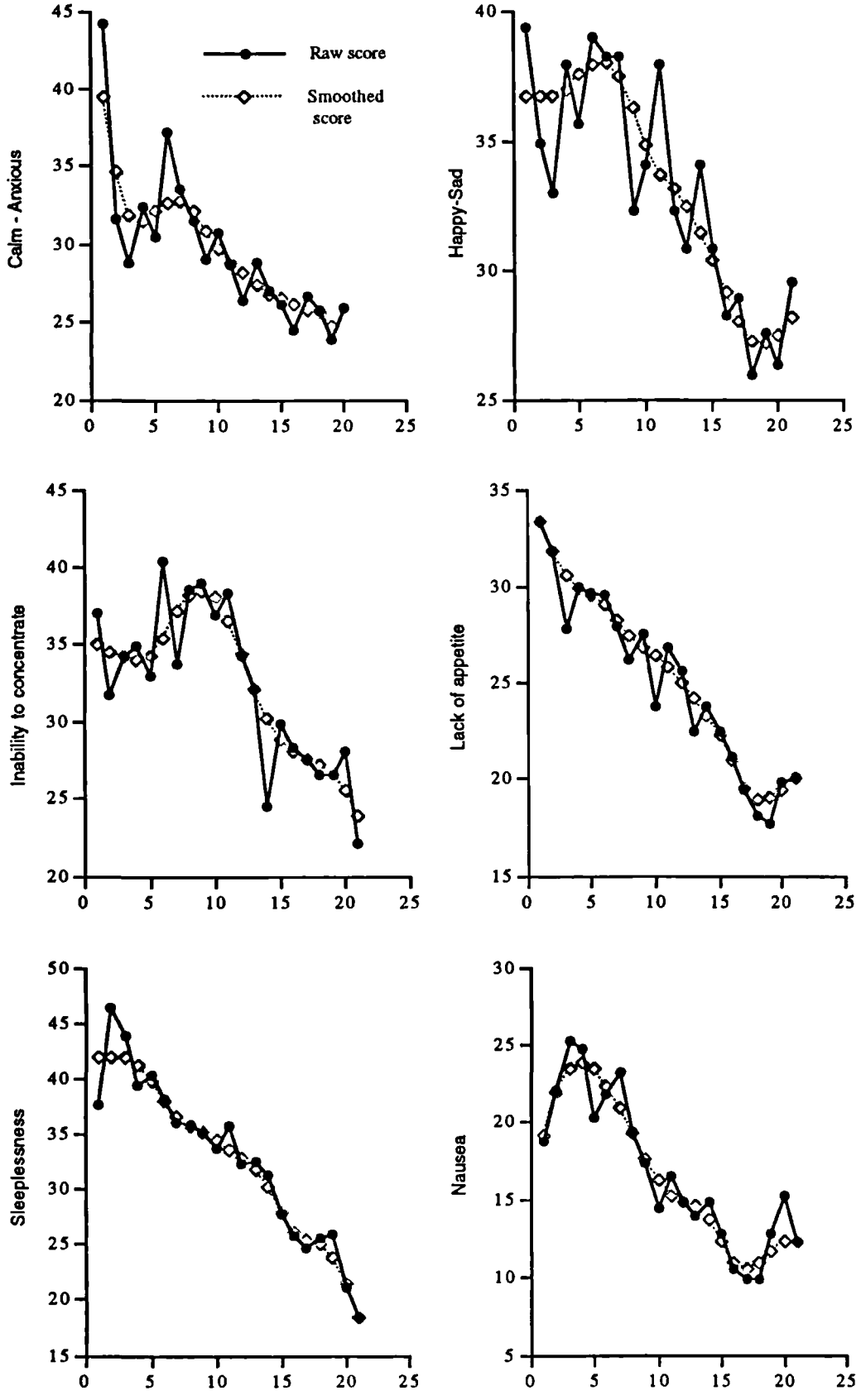




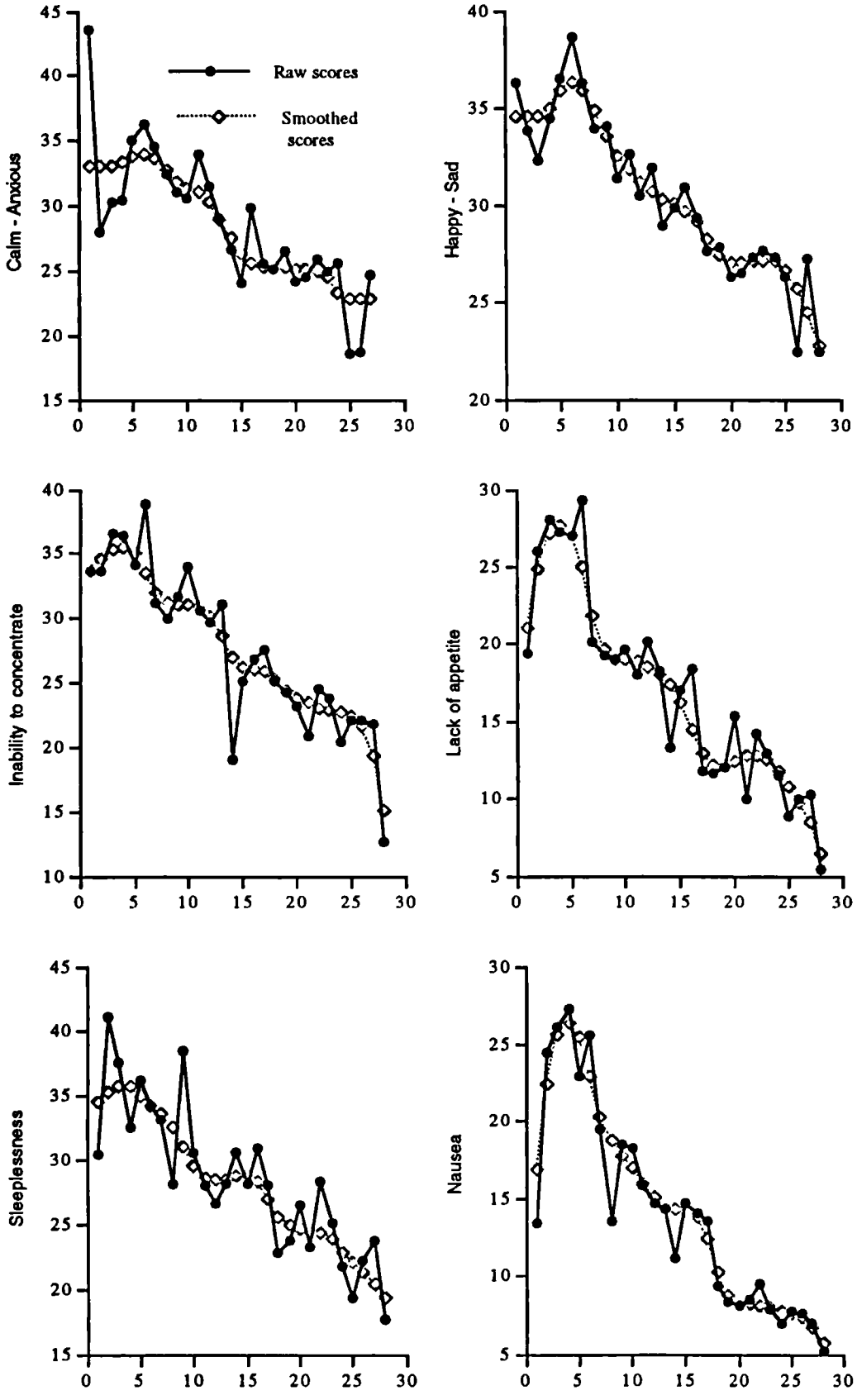




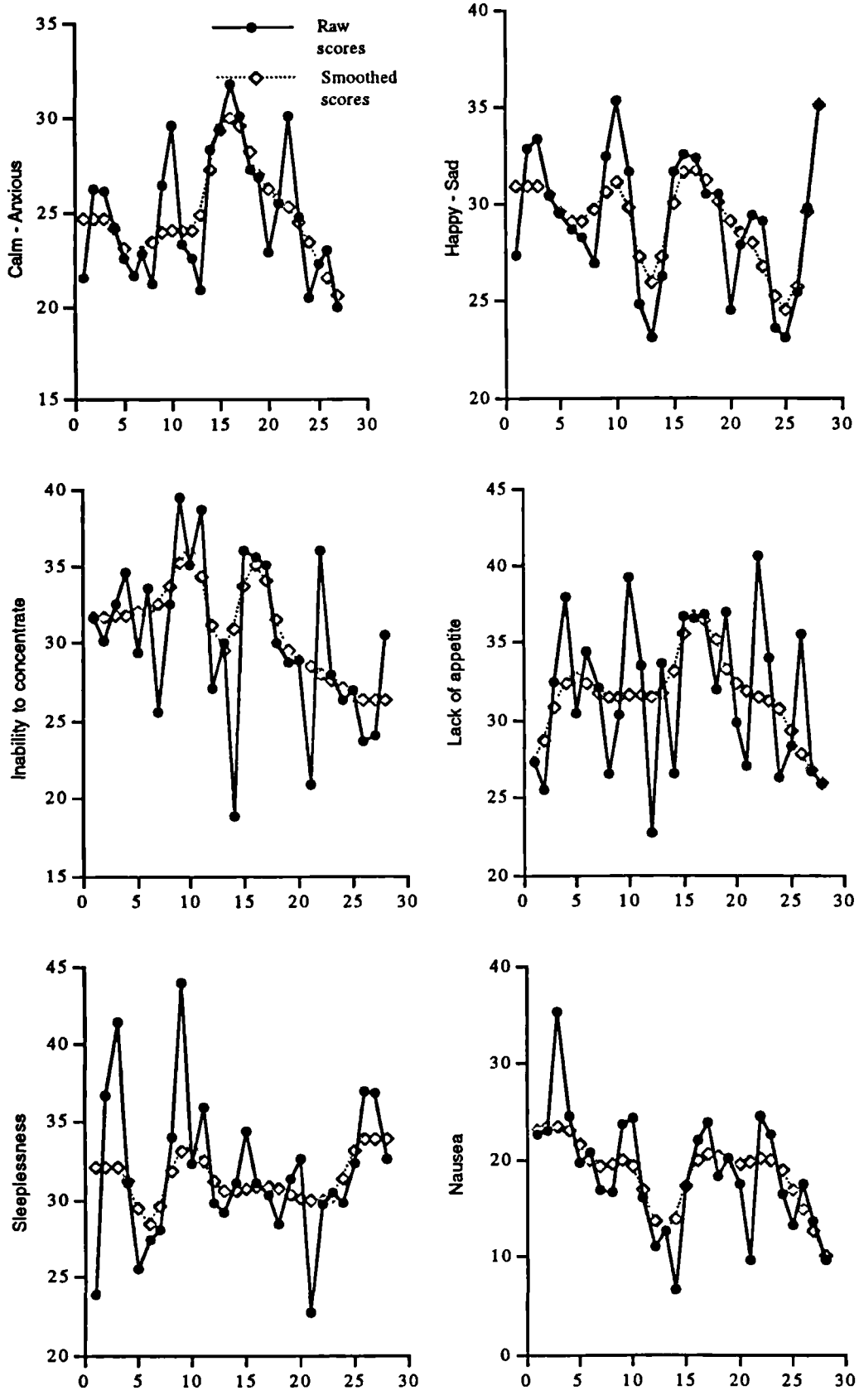
Appendix O Time plots of raw and smoothed daily diary items of subjects receiving a 21-day cycle of chemotherapy



Appendix P Time plots of raw and "smoothed" daily diary items of subjects receiving a 28-day cycle of chemotherapy



Appendix Q Time plots of raw and "smoothed" daily diary items of subjects receiving weekly chemotherapy



Fatigue in cancer patients: a review of the literature

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Fatigue in cancer patients: a review of the literature

This paper reviews the research literature concerning fatigue in cancer patients, evaluating the quality of the evidence, thus helping to focus the direction and methodological rigour required in future investigations. Since fatigue in this population has been attributed to several mechanisms these will be discussed. The prevalence of fatigue in cancer patients will then be documented. An overview of what is currently understood about fatigue in cancer will follow. Based on the literature, conceptual and methodological difficulties will be described. Finally, gaps in understanding will be identified. Suggestions for future research will be formulated and potential interventions to decrease feelings of fatigue explored.

Keywords: fatigue, cancer.

INTRODUCTION

Cancer and its treatment are characterized by a variety of possible symptoms such as pain, shortness of breath, nausea, loss of appetite and fatigue. Of these, investigators have found that patients report fatigue as the most disturbing symptom experienced during treatment (Rhodes *et al.*, 1988). It causes the greatest amount of interference with self-care (Fernsler, 1986) and has impact on such areas as the ability to perform household tasks and enjoyment of leisure activities (Todres & Wojtuik, 1979).

THE BASIS OF CANCER FATIGUE

Fatigue is multifactorial and multidimensional; there are biological, psychological, social and personal factors that possibly influence onset, impact, expression, duration and severity of the fatigue experience. Most of the research on fatigue in cancer patients has not clearly identified specific correlates of fatigue. It is not clear how the direct effects of cancer, symptoms related to cancer, effects of cancer treatment and the strain of dealing with cancer, interact to generate or exacerbate fatigue. A combination of mechanisms are likely. All are potentially relevant to explaining some aspects of the fatigue experienced by the individual with cancer. Presently, the most reasonable approach to exploring the aetiology of fatigue in individuals with cancer is to consider multiple factors (Nail, 1990).

Somatic mechanisms

Mechanisms most likely to influence fatigue in cancer patients include the liberation of intracellular products and metabolites resulting from cell lysis and necrosis of the tumour mass, following chemotherapy and radiotherapy. It has recently been hypothesized that mechanisms may involve changes in skeletal muscle protein stores resulting from endogenous or treatment administered tumour necrosis factor (St Pierre *et al.*, 1992). Fatigue may prove to be a manifestation of aberrations in energy availability and expenditure frequently encountered with cancer and its treatment, such as anorexia, cachexia and changes in metabolism (Kaemfer *et al.*, 1986; Lindsey, 1986).

Alteration in the body's immune status (bone marrow depression possibly resulting in infection and fever) and ability to obtain and maintain oxygen levels induced by a state of anaemia or dyspnoea are frequently believed to induce fatigue (Maxwell, 1984). However, evidence for this link has not revealed consistent evidence. Fluid and electrolyte imbalance due to the disease or treatment could potentially affect neurotransmission and muscle force. This could result in fatigue and lethargy. Insomnia is suggested to be a common occurrence in cancer patients (Kaye *et al.*, 1983; Silberfarb *et al.*, 1985). No detailed investigation of the relationship between alterations in sleep and rest patterns and fatigue have been undertaken, and the literature pertaining to sleep disturbance is contradictory (Beszterczey & Lipowski, 1977; Lamb, 1982).

Symptoms

The constellation of symptoms, side-effects and medications used to control them which cause discomfort may interact to produce fatigue. Fatigue does seem to be associated with pain (Blesch *et al.*, 1991). Arathuzik (1991) in describing the pain experience of patients with metastatic breast cancer fatigue elicited fatigue as a common concern in relation to the pain experience. It also interfered with daily household and leisure activities. Lung cancer patients are acknowledged by clinicians as being constantly tired and this appears to be supported empirically. Brown *et al.* (1986) related fatigue with the sensation of dyspnoea and it was suggested that dyspnoea may be construed synonymously with fatigue by patients with lung cancer.

Substantial evidence exists that cancer chemotherapy provokes substantial levels of emotional distress (Meyerowitz *et al.*, 1979; Burish *et al.*, 1983; Silberfarb *et al.*, 1983) and the processes that provoke distress have been elaborated by Leventhal *et al.* (1986). In this team's research a major source of physical and emotional upset proved to be the combination of side-effects. Difficulty with treatment, disruption in social and work life, and emotional distress and number of side-effects all correlated. The amount of distress generated was mediated by psychological processes such as interpretation of and coping with side-effects of treatment. Munkres *et al.* (1992) more recently addressed the role played by appraisal and the personal meaning of a situation and the resources available for dealing with it in directly mediating the effects of distress.

Leventhal and his co-workers suggested that some side-effects give rise to as much distress as the disease itself, because they are reminiscent of it, serving as strong reminders of cancer. The side-effect of tiredness might echo the disease because it accompanies most illnesses and might be confused with cancer. Limited support for this assumption was gained, because there was a greater likelihood for vague, long-term side-effects, such as tiredness, to be associated with emotional distress. However, it was recognized that as tiredness can also be the result of emotional distress; it is plausible that such distress exacerbates or causes this state which the patient labels as a treatment effect. Temporal relationships between side-effect severity and distress remain unclear, and should be explored in a longitudinal study to clarify causal relationships.

Psychological mechanisms

The above discussion supports the need to take into account the psychological component of fatigue. Emotional vulnerability has been observed by Weisman (1976) in newly diagnosed cancer patients and associated with fatigue. A variety of emotional responses and ineffective coping strategies are frequently reported in cancer patients (anxiety, depression, confusion, fear and anger). Such responses and the endurance of heavy stress over prolonged periods of time necessitating active coping associated with particularly distressing side-effects may contribute to fatigue (Nerenz *et al.*, 1982; Knobf, 1986; Blesch *et al.*, 1991). The mental effort required to cope with the intense and competing demands imposed by a diagnosis of cancer may lead to attentional fatigue, Cimprich (1992a) has demonstrated a decline in the capacity for attention and concentration in women undergoing treatment for breast cancer in the initial phases of illness.

Collectively, the evidence suggests that psychological distress is a potentially important variable to consider in studies of fatigue in cancer patients. Prolonged stress is proposed by Aistairs (1987) as the main cause of fatigue in the person with cancer. Such responses may not only cause, but also result in persistent fatigue. In cancer depression and fatigue may co-exist, both resulting from identical biological factors (Hayes, 1991). More systematic studies need to be performed to investigate the relationship between depression, anxiety and the fatigue experience of cancer patients. The characteristics of the individual, including motivation, beliefs and attitudes, and the individual's perception of cancer should be considered.

Social support

Resource-related factors such as the perceived le-

social support may be vital. It is important to understand the role social support plays in the perception and management of symptoms such as fatigue. The relationship between level of daily activities/functional ability and fatigue in individuals undergoing treatment for cancer has not been systematically evaluated. Thomas & Dodd (1992) developed a model for morbidity in ambulatory cancer patients and, of the indices selected to reflect the functional domain (functional status, social resources, economic resources, vigour and fatigue), total function correlated with all the indices, although less so with vigour and fatigue. Both vigour and fatigue correlated with all the indices, except social resources. The results of this study should be viewed with caution as they are based on a secondary analysis of pre-existing data, and the instruments used in the original study may not have been ideally suited to measure the variables being studied in the construction of the model. Several studies have documented problems cancer patients experience in maintaining functional performance and have suggested a relationship between fatigue and disruption in functional performance status (Kubricht, 1984; King *et al.*, 1985; Rhodes *et al.*, 1988).

COPING RESPONSES TO FATIGUE

Fatigue may appear unalterable to the patient, family and health professional, becoming synonymous with the challenge of living with cancer and its treatment. In living with fatigue patients develop many strategies and skills of their own over time. There is potential to learn from studying the actual coping practices of patients who experience persistent fatigue.

Strategies patients employ to deal with fatigue have been reported in the self-care research (Dodd, 1988a,b; Rhodes *et al.*, 1988; Nail *et al.*, 1991; Robinson & Posner, 1992) and in some of the descriptive and instrument development fatigue studies (Jamar, 1989; Piper *et al.*, 1989a). What one patient finds useful may be of no benefit to another, although commonly recurring themes such as taking naps and resting, going to bed earlier and keeping busy to keep the mind off fatigue, feature in the majority of the responses and have been supported in recent research undertaken by the present author (Richardson, 1994). However, these are only partially effective in ameliorating the problem.

Robinson & Posner (1992) indicated that nurses and family members had little idea which interventions patients themselves indicated would be beneficial in reducing fatigue. A possible relationship between a patient's representation of fatigue and his/her selection of strategies has not been investigated. We should determine whether the coping strategies are developed from a patient's own experience or were learned from others. The previous research by Dodd reveals that health-care professionals possibly play only a small part in this.

There is no differentiation in the current research between immediate strategies and long-term alterations that are incorporated into the life-style. The experience of episodic fatigue versus persistent fatigue and other differences in the fatigue experience should result in researchers comparing and contrasting strategies used at differing stages in the disease and treatment career of cancer patient. The efficacy of preventive versus reactive strategies should also be documented.

INTERVENTIONS FOR FATIGUE IN CANCER PATIENTS

Some of our most common interventions are based on little or no empirical evidence for people with cancer. Results from earlier studies indicate that patients do not always expect fatigue to be a problem. Accurate and relevant preparatory information on the impending experience of what to expect in terms of fatigue during and following treatment could enhance the patient's ability to cope. Other studies have illustrated the practical value of such information in facilitating coping (Johnson & Leventhal, 1974), but we have little research to inform us of the incidence, time of onset and duration of fatigue or efficacy of self-care activities routinely suggested to patients. Skalla & Lacasse (1992) have produced specific patient education material for fatigue.

In healthy individuals, it is generally assumed that exercise is effective in reducing fatigue (Thayer, 1987). Exercise is often recommended as an integral component of cancer rehabilitation (Shaw *et al.*, 1962; MacVicar & Winningham, 1986; Winningham & MacVicar, 1988; MacVicar *et al.*, 1989; Winningham *et al.*, 1989; Winningham, 1991; Young-McCaughan & Sexton, 1991). So far this assumption has been supported by serendipitous findings and tested with breast cancer patients in preliminary studies only. Results suggest that fatigue may be reduced by an exercise programme (Questad *et al.*, 1982; Questad, 1983; Winningham *et al.*, 1985; MacVicar & Winningham, 1986; MacVicar *et al.*, 1989; Young-McCaughan & Sexton, 1991), but is subject to dispute (St. Pierre *et al.*, 1992).

Considering the hypothesized relationship of stress with fatigue in cancer patients described by Aistairs (1987), stress management resulting in a reduction of anxiety and promotion of coping are important outcomes that may decrease fatigue. Studies evaluating the effectiveness of

psychotherapeutic interventions for cancer patients have found decreased fatigue scores to result (Spiegel *et al.*, 1981; Forester *et al.*, 1985). Therefore, interventions aimed at reducing emotional distress or enhancing coping responses may be an effective way to decrease feelings of fatigue. Johnson *et al.*'s (1988) study with radiotherapy patients, although not directed specifically at the symptom of fatigue, suggested that the provision of information directed at preparing patients to view symptoms as a normal part of treatment rather than a sign of disease progression when appropriate may be beneficial. Diversional activity and its utility in enhancing coping has been explored by Radiewicz & Schneider (1992).

Unfortunately, there seems little to recommend because, at the present time, fatigue interventions have not been adequately tested in cancer patients. A multi-method fatigue therapy programme is likely to be the most effective and may include energy conservation activities, a planned exercise programme, stress reduction strategies and nutritional counselling. Interventions offered will need to be tailored to the needs of the individual patient.

PREVALENCE OF CANCER FATIGUE

Chemotherapy

The prevalence of fatigue in cancer patients undergoing chemotherapy has been estimated. Coates *et al.* (1983) surveyed a varied group of chemotherapy patients asking them to identify, and rank the physical and non-physical side-effects. Experiencing constant tiredness was ranked highly overall, but its relative importance to other symptoms varied on a number of factors. Meyerowitz *et al.* (1979), whilst outlining the psychosocial implications of adjuvant chemotherapy in breast cancer patients, reported fatigue in 96% of the sample ($n = 50$). It was heralded as the most common and disruptive symptom. Frequent and dramatic changes in activity levels were often the result, a finding supported by Frank-Stromborg & Wright (1984). Studies involving patients receiving chemotherapy for a variety of different types of cancer report incidence ranging from 59 to 82% (Nerenz *et al.*, 1982; Cassileth *et al.*, 1985; Nail & King, 1987; Nail *et al.*, 1991). Fatigue has also been identified to be the most *distressing* side-effect reported by patients receiving chemotherapy (Knobf, 1986; Strauman, 1986). The predominance of fatigue in cancer patients treated with chemotherapy is also supported through non-statistical descriptive accounts and clinical observations (Fernsler, 1986; Rhodes *et al.*, 1988).

Cassileth *et al.*'s (1985) study illustrated that patients about to receive chemotherapy consistently underestimated the possibility that they would experience side-effects including feeling tired. The frequency of expected side-effects was much greater than patients anticipated. Tiredness was one of the most common reported side-effects. Patients' expectations failed to predict their occurrence or severity.

Related to this, Teirney *et al.* (1989) in a detailed descriptive study of breast cancer patients receiving chemotherapy, revealed discrepancies between the side-effects that patients had expected would be most difficult to cope with and those that they actually found in reality to be the most problematic. The focus of the study was alopecia. However, a considerable amount of data were collected on other aspects. Tiredness was singled out as the side-effect most often reported. It was reported by 87.5% of the sample ($n = 60$) at any stage of treatment, generating a great deal of comment and concern among patients. Only a couple of women had expected tiredness to be so frequent or so problematic to cope with, and only half had been forewarned. It appeared to become more problematic as treatment progressed, but interestingly in this study, it was one of the few side-effects perceived to be under the patient's control.

Radiotherapy

There is substantial evidence to suggest that fatigue is also an important clinical problem for patients undergoing radiotherapy. The reported incidence of fatigue as a side-effect in studies where patients receive external or intracavitary radiation has been documented, ranging from 65 to 100% (Peck & Boland, 1977; Kubricht, 1984; King *et al.*, 1985; Oberst *et al.*, 1991; Nail, 1993). Fatigue appears to peak and wane over the course of treatment (Greenberg *et al.*, 1992). Among subjects receiving radiotherapy to specific anatomic sites, interviewed weekly during the course and once a month for 3 months after the completion, the highest incidence of fatigue was found in patients receiving radiotherapy to the chest (King *et al.*, 1985).

Biological therapy

In a review of the use of interferon, fatigue was reported to be the most prevalent symptom, the most important dose-limiting toxic effect, and the most difficult side-effect to manage (Quesada *et al.*, 1986). Anecdotal information seems to indicate fatigue is more severe in this group of patients than in those receiving any other treatment modality such as chemotherapy or radiotherapy. It has

been consistently documented that patients receiving biotherapy (interferon, interleukins, colony-stimulating factors and tumour necrosis factor) experience fatigue as a significant and, at times, dose-limiting side-effect, although information is limited about fatigue patterns in the biotherapy literature. Piper *et al.* (1989b) synthesized what is currently known on this, based mainly on clinical observation and unpublished data.

Surgery

With the exception of Cimprich's (1992a,b; 1993) work, studies of surgical patient fatigue do not involve patients with cancer. Though not specific to cancer patients, an abundance of evidence documenting the occurrence of fatigue after surgery has been presented in a review by Rhoten (1982). The adjustment to low energy levels required of patients and their families on return home has been confirmed (Oberst & James, 1985). Fatigue after surgery is particularly relevant to cancer patients who receive adjuvant therapy in that they have often not recovered prior to further treatment commencing. The possible cumulative effects of sequential treatments may increase the risk for the occurrence of fatigue in such a population.

Following treatment

Evidence that fatigue continues after radiotherapy and chemotherapy treatment protocols have been completed is limited (Eardley, 1986; Fobair *et al.*, 1986; Knobf, 1986; Devlen *et al.*, 1987; Bloom *et al.*, 1990; Berglund *et al.*, 1991) and has been the sole focus of only one small project (McArthur, 1992). Fatigue remained a significant problem for many months. An interest in this time period in the *survivorship* and *rehabilitation* literature may reveal more detailed accounts of the influence of fatigue on these patients' lives. We probably underestimate the residual effects of therapy. Comparison to a healthy control population is needed and identification of predictive factors sought in those most likely to be affected by low levels of energy.

Summary

Many patients with cancer have identified fatigue as a frequent and significant side-effect. To date, there have been few studies to register systematically the number of cancer patients experiencing fatigue which also take into account the stage of the disease process and the extent of the problem. Most studies reporting the incidence of fatigue as a side-effect of cancer treatments have limitations in that they include subjects presently under treatment as well as those who have completed treatment; subjects are interviewed only once so it is impossible to establish any pattern and patients with a variety of tumours, treatments, sites of treatments and stages of disease (Nail & King, 1987) are included. In spite of these limitations it can be concluded that there is strong evidence to suggest that fatigue is a prevalent problem among patients receiving treatment for cancer and probably varies according to the phase and time of treatment (Haylock & Hart, 1979; De Haes *et al.*, 1987).

PRESENT STATE OF KNOWLEDGE OF FATIGUE IN CANCER PATIENTS

The following section appraises the nursing research literature directly concerned with fatigue in cancer patients (see Tables 1–4) because their cumulative findings are of direct value to practice. Irvine *et al.* (1991) and Potempa (1993) have previously critically appraised the research literature on fatigue in the individual with cancer. However, they fail to differentiate in their review between studies which focus on fatigue as the main variable of the study and those in which it is not the main focus of the research.

Nature of studies

Studies investigating fatigue in cancer patients have been restricted primarily to those patients undergoing treatment with chemotherapy or radiotherapy. Less is known about the correlates of fatigue or the occurrence of fatigue in cancer patients before and after treatment. Research studies to explore the topic explicitly may be categorized as follows:

1. Those describing fatigue in a specific group of cancer patients, e.g. Davis (1984) and Jamar (1989)
2. Comparative studies describing different groups of cancer patients, the independent variable being the type of treatment, e.g. Blesch *et al.* (1991) and Haylock & Hart (1979)
3. Studies comparing cancer patients to non-cancer patients; either patients with other diseases or healthy individuals, e.g. Pickard-Holley (1991).

A primary question often posed by practitioners is 'Does fatigue differ in these groups?'. From the studies conducted to date we are unable to conclude that differences between groups of cancer patients are primarily related to certain factors. It is commonly assumed that cancer and cancer treatment has a severe and negative effect on fatigue. Support for the assumption that fatigue is worse in

Table 1. Summary of cancer nursing research concerned with fatigue in chemotherapy patients

Study ref.	Sample and aims	Study design	Instruments	Main findings
Rhodes *et al.* (1988) Patients' descriptions of the influence of tiredness and weakness on self-care abilities	Cancer patients who have received 6 pulses of chemotherapy (CT) $n=20$ To examine retrospectively, utilizing an interview schedule, the relationship between patients' self-reported symptoms and their self-care activities during anti-neoplastic chemotherapy, and to describe these findings within the Self-Care Defecit Theory of Nursing	Descriptive Retrospective	Self-care telephone interview schedules A and B (A) Regarding self-care and symptoms (B) Regarding self-care and fatigue	Tiredness and weakness were identified as the symptoms that most interfere with self-care activities in interview A. 9 out of 11 subjects identified self-care activities on the day of CT and day following CT as limiting the expenditure of energy. These were categorized into limiting the expenditure of energy by planning/ scheduling activities, decreasing non-essential activities, and increasing dependence on others for home management, transport and care dependence
Pickard-Holley (1991) Fatigue in cancer patients—a descriptive study	Ovarian cancer patients (stage IIB–IIIC) receiving CT $n=12$ Healthy female controls $n=12$ To examine whether there were any relationships between fatigue, and various physical and psychological factors in women undergoing treatment for cancer	Descriptive/ correlational & comparative Prospective (Day 1, 7, 14 & 21) and cross-sectional (varying pulses of CT)	Rhoten Fatigue Scale (RFS) Beck Depression Inventory (BDI) Gynaecology Oncology Group Performance Scale Kamofsky Performance Scale CA125 weight change and other lab values	Weak to moderate relationships found between levels of fatigue and CA125 levels. As CA125 levels decrease fatigue also decreases. There was no significant difference between the mean fatigue score of the patient and control group. The fatigue trajectory was found to peak at Day 7 and slowly decline during the remainder of the 28-day cycle. No significant relationship was found between fatigue and age, stage of disease, course of treatment or depression
McArthur (1992) A study of fatigue in cancer patients receiving chemotherapy	$n=35$ Group A receiving CT $n=17$ Group B completed CT attending out-patients $n=18$ 1. To examine the extent of the problem of fatigue in a cancer population 2. To determine what effect chemotherapy has on the individual's level of fatigue 3. To identify perceived causes of fatigue and relief measures 4. To develop a conceptual framework which may be used to provide effective nursing interventions	Descriptive/ correlational & comparative Prospective Group A prior to 1st CT, at nadir and prior to 2nd CT Cross-sectional Group B on one occasion	Piper Fatigue Scale (PFS)	94% of group A had some degree of fatigue, and 50% in group B. No statistical evidence to suggest any significant difference between the mean fatigue scores of group A prior to CT and Group B. No statistical difference in fatigue scores between ovarian and non-ovarian patients. Statistically significant increases in affective and severity dimensions in Group A fatigue scores over time
Jamar (1989) Fatigue in women receiving chemotherapy for ovarian cancer	Women receiving out-patient CT For ovarian cancer (stage I–IV) $n=16$ The purposes of the study were to obtain descriptions of the phenomenon of fatigue in individuals receiving chemotherapy, to determine if there is an identifiable fatigue pattern related to the chemotherapy cycle, and to determine the effect of fatigue on activity level and life-style on the individual	Descriptive/ correlational Cross-sectional	Semi-structured interview including items on sleep pattern, activity level, accounts of the fatigue experience and strategies used to relieve fatigue Profile Of Mood States-Short Form (POMS-SF) Symptom Distress Scale (SDS) Pearson Byars Fatigue Feeling Checklist (PBFFC)	A pattern of fatigue related to the chemotherapy cycle emerged, worse in the first week following CT lessening prior to next pulse of CT. Symptom distress was related to increased levels of subjective fatigue. Physical descriptors, emotional descriptors and descriptors related to changes in energy level were used to describe fatigue. Levels of fatigue were significantly related to living arrangements, single parents and women without assistance at home generally had higher levels of fatigue. The PBFFS significantly correlated with total SDS ($r=0.6249$, $P<0.001$) and with nausea and fatigue subscales ($r=0.5811$, $P<0.01$, $r=0.8656$, $P<0.001$) and the POMS-SF total score ($r=0.6405$, $P<0.01$)

Table 2. Summary of cancer nursing research concerned with fatigue in biological therapy patients

Study ref.	Sample and aims	Study design	Instruments	Main findings
Davis (1984) Interferon-induced fatigue	Malignant melanoma patients receiving IFN-alpha 2 I.V. daily for 4 weeks $n = 16$ To identify the degree of fatigue experienced and the impact on functionability of patients with malignant melanoma receiving IFN-alpha 2	Descriptive/ correlational Prospective (Days 0, 12 and 26)	Pearson Byars Fatigue Feeling Checklist (PBFFC) Fatigue Symptom Checklist (FSC) Sickness Impact Profile (SIP)	Significant correlations were found between the cumulative dose of IFN, the fatigue scores and no of fatigue symptoms. Significant negative changes occurred in sleeping, eating, mobility and social activity patterns. Most frequently reported physical symptoms of fatigue were leg weakness and a need to lie down, while difficulty thinking and impatience with others were frequent mental symptoms
Rieger (1987) Interferon-induced fatigue: a study of fatigue measurement	Cancer patients receiving IFN alpha and gamma by variable route and dose $n = 30$ To describe changes in fatigue, functional status, and muscular strength as experienced by cancer patients receiving interferon therapy	Descriptive/ correlational Prospective (pretherapy, 1 week and 1 month post-therapy	Pearson Byars Fatigue Feeling Checklist (PBFFC) Functional Living Index–Cancer (FLIC) Jamar Hand Held Dynamometer	No significant differences were found over time in subjective fatigue, functional status and muscular strength. Significant negative correlations were found between the PBFFC and the FLIC
Robinson & Posner (1992) Patterns of self-care needs and interventions related to biological response modifier therapy: fatigue as a model	Cancer patients who have had at least one treatment receiving IFN-alpha, TNF or IL-2 and a designated family member and nurse $n = 16$ patients The objectives of the study were: (1) to conduct a pilot study of the High-Intensity Self-Care Needs and Interventions Survey (2) to describe the patterns of self-care needs and interventions among patients receiving in-patient or out-patient biotherapy	Comparative Cross-sectional	Analysis Of High Intensity Self-Care Needs and Interventions Survey	Patient and family members responses correlated well In several parameters including degree and duration of fatigue nurses' perceptions did not correlate at all with patients. There was minimal agreement among patients, family members and nurses' responses as to the interventions that could be used by others to help patients cope with fatigue. It was considered that the instrument should be shortened and questions clarified

this population than in others is lacking. To test this hypothesis comparative studies need to be performed with cancer patients and healthy controls. Marked differences between groups will only be uncovered if objective, sensitive indicators are utilized. With only one exception (Pickard-Holley, 1991) the studies have not included a comparison group permitting fatigue in cancer patients to be compared with other populations. This particular study failed to demonstrate any difference between a small number of cancer patients and a healthy control group. Findings such as these may be due to the operationalization of the concept, methodological aspects of the study or psychological mechanisms that have influenced fatigue, but which have not been taken into account.

Defining and operationalizing the concept of fatigue

The meaning attributed to the concept of fatigue is rarely made clear, nor how the definition has been interpreted within a particular study. A number of terms may be used interchangeably. Fatigue is often operationalized as the subjective feeling of tiredness and lack of physical energy. Fatigue is considered to be a multidimensional construct, but this is not always reflected in the choice of measurement strategies. Researchers also assume that certain spheres of life are affected by fatigue. As a clear framework is lacking and the dimensions of fatigue that should be considered unclear, the choice of areas is based on intuition. Authors generally include the presence of other symptoms, psychological well-being and the performance of activities. Social functioning or social support may account for unexplained variance. Material areas, such as the impact of fatigue on economic welfare should not be neglected. Choice of areas and operationalization of the concept is not consistent, and this creates difficulties in making comparisons.

Subjects and methods

Three studies of radiotherapy patients have consistently found that the prevalence of fatigue increases over the course of radiotherapy (Haylock & Hart, 1979; Kobashi-

Table 3. Summary of cancer nursing research concerned with fatigue in radiotherapy patients

Study ref.	Sample and aims	Study design	Instruments	Main findings
Haylock & Hart (1979) Fatigue in patients receiving localized radiation	In-patients and out-patients with cancer at various sites $n=30$ The major questions of the study were: (1) does localized RT precipitate a fatigue which exhibits a pattern of intensity related to the duration of treatment? (2) does localized RT precipitate a state of fatigue which is characterized by a specific constellation of symptoms?	Descriptive/ correlational & comparative Prospective (each day of radiotherapy [RT])	Fatigue Symptom Checklist (FSC) Pearson Byars Fatigue Feeling Checklist (PBFFC)	There was a consistent drop in fatigue scores on Sundays throughout the study. Lung and breast cancer patients experienced a significant change in baseline fatigue to the highest fatigue score reached ($P<0.068$). Time since surgery was significantly related to mean fatigue levels ($r=0.34$, $P<0.07$). Weight was negatively correlated with fatigue ($r=-0.54$, $P<0.002$). Subjects who underwent the most lengthy regimes had the greatest change in fatigue levels. On the FSCL the symptoms tired in whole body, tired legs, heavy head, wanting to lie down and feeling ill correlated with fatigue levels experienced
Kobashi-Schoot *et al.* (1985) Assessment of malaise in cancer patients treated with radiotherapy	Cancer patients receiving out-patient RT $n=95$ To develop a quantitative approach to assess malaise	Descriptive/ correlational & comparative Prospective (each Monday and Friday over 3 weeks)	Questionnaire: (A) Fatigue Symptom Checklist (FSC) (B) Checklist For Cancer Patients (CCP) (C) Malaise Scale–4 visual analogue scales (D) Ill–well dimension scale (E) Questions on hours of rest during the day and daily activities	Physical fatigue correlated highest with the no. of hours rest during the day ($r=0.58$, $P<0.001$). Ill–well dimension correlated with malaise ($r=0.74$, $P<0.001$). ANOVA revealed there was a significant increase in physical fatigue and malaise over the course of RT. Patients with lymphoma and uterine cancer suffered less following a weekend; this was not observed for breast and bladder patients. There was no change in emotional state and no correlation of any of the variables measured with age
Piper *et al.* (1989a) The development of an instrument to measure the subjective dimension of fatigue	Breast or lung cancer out-patients receiving RT $n=50$ 1. To explore the initial psychometric properties of an instrument constructed to measure multiple dimensions of fatigue 2. To describe the baseline patterns of fatigue experienced by radiation therapy patients using the above tool	Descriptive/ correlational Retrospective	Piper Fatigue Scale–Baseline (PFS-B) Profile Of Mood States (POMS) Fatigue Symptom Checklist (FSC)	Moderate evidence for discriminant and convergent validity of the PFS was found. The majority of patients had experienced an increase in fatigue score (PFS) during the 6 months before diagnosis, but most patients reported their fatigue as mild, intermittent and acute. Most patients believed that illness was the cause of their fatigue. Sleep and lying down for short periods were reported as effective in relieving fatigue. The average no. of FSC symptoms reported was 6.36. Stage of disease did not affect the number, type, or intensity of fatigue symptoms significantly. Lung cancer patients tended to start RT at a higher level of fatigue than breast cancer patients

Schoot *et al.*, 1985; Piper *et al.*, 1989a). The pattern varies, occurring intermittently at the start and becoming continuous as treatment progresses. More is known about the prevalence, duration and pattern of fatigue in patients receiving radiotherapy than other treatment groups (Irvine *et al.*, 1991). Four studies have been conducted with a sample of patients receiving chemotherapy. A decline in fatigue scores is generally recorded after drug administration has concluded.

Differences in methodology and treatments preclude meaningful comparisons, although it may be concluded that fatigue is troublesome. Contributing to a lack of knowledge are a number of measurement issues. Four groups of studies are distinguished. First, some authors developed *ad hoc* questions to measure fatigue, and failed to report validity and reliability of the instruments used. A second group of investigators used measures developed in other fields to study fatigue in cancer patients. These

Table 4. Summary of cancer nursing research concerned with fatigue in radiotherapy and chemotherapy patients

Study ref.	Sample and aims	Study design	Instruments	Main findings
Blesch *et al.* (1991) Correlates of fatigue in people with breast or lung cancer	$n = 77$ Lung cancer patients ($n = 33$) and breast cancer patients ($n = 44$) receiving CT and/or RT as in- or out-patients The study aimed to: (1) discern behavioural, physiological and biochemical factors that may be linked with subjective ratings of fatigue reported by adults undergoing active treatment (2) examine the psychometric properties of three instruments used to measure fatigue	Descriptive/ correlational Cross-sectional	Rhoten Fatigue Scale (RFS) and Checklist (ROC) Profile Of Mood States–Short Form (POMS-SF) Medical record audit for values of biochemical and physiological correlates of fatigue Questionnaire on pain, sleep and social support	Fatigue was present in 99% of sample; 64% rated fatigue as moderate to severe. Significant correlates of fatigue intensity were pain severity ($r = 0.48$, $P < 0.0001$), total mood disturbance ($r = 0.48$, $P < 0.0001$) and several subscale scores of POMS-SF. Mean fatigue levels between breast and lung patients were not significantly different. Fatigue did not correlate with any biochemical parameters and only one physiological correlate, pain. Duration of illness positively correlated with fatigue in breast patients, but not in lung patients. The ROC data was found to be very inconsistent and therefore not used
Piper *et al.* (1990) Fatigue—transcultural implications for nursing interventions	American and South Korean Breast Cancer patients receiving RT or CT $n = 74$ (American) $n = 11$ (Korean) 1. To investigate fatigue patterns and self-initiated interventions in Korean women with breast cancer 2. Compare findings to fatigue patterns and interventions documented in North American women with breast cancer	Descriptive/ correlational & comparative Prospective (first 3 weeks of RT and weekly during first 2 pulses of CT)	Profile Of Mood States (POMS) Piper Fatigue Scale (PFS) (Times 1–3, weekly) Korean women Hae Ok Lee Checklist (HOFC) (Times 1–3, weekly)	Average total fatigue score of patients (30.5) on HOFC slightly lower than average fatigue scores of healthy workers in a previous study. No change over time in POMS for RT patients or for Korean women receiving CT. RMANOVA revealed American women receiving CT total mood disturbance scores were significantly greater on day 1 of 2nd pulse of CT (F, 10.49; $P < 0.0001$), and significantly less vigour was reported (F, 10.750; $P < 0.0001$). Total fatigue scores on the PFS did not vary between two groups or by treatment. Fatigue scores did not appear to change over time in the Korean sample; in the American sample in women receiving CT, the mean sensory scores and total fatigue scores changed significantly over time

scales refer to psychological adjustment and functional status such as Profile of Mood States (McNair *et al.*, 1992) and the Sickness Impact Profile (Bergner *et al.*, 1981). Measures used to study fatigue in other populations such as industrial workers comprise a third group [the Fatigue Symptom Checklist (Yoshitake, 1971) and Pearson Byars Fatigue Feeling Checklist (Pearson & Byers, 1956)]. In a fourth type of study, specific instruments have been developed to measure fatigue in cancer patients [the Piper Fatigue Scale (Piper *et al.*, 1989a)]. Some reliability and validity testing has been performed for most of these instruments in the latter three groups, but is limited. The advantages and disadvantages of various self-report methods need to be explored in some detail with consideration to what constitutes the best time to measure fatigue in cancer patients.

Studies cover a wide range of patient groups, but samples are small and differ along medical dimensions: the type of tumour, the stage of disease, the treatment received and in the differing points in treatment. Small sample size makes it difficult to discern genuine differences. A second issue relates to the control of background variables. Medical parameters are assumed to be the independent variables influencing the fatigue of cancer patients. Only in a few investigations have the groups been compared with respect to such variables as age, sex and time elapsed since treatment. These may explain a substantial part of the variance of the dependent variable fatigue.

Thus, research methods do not seem altogether adequate in many of the reviewed studies. Some have small sample sizes, many do not consider intervening variables, and the instruments used have not always proved reliable and valid. The design of studies has not always been sufficiently rigorous.

Theoretical notes

Strategies to develop theory related to fatigue need to be identified. These could be used to guide research and practice. The ultimate goal of such theories will be to identify and predict which patients are at high risk for fatigue in order to test specific interventions that prevent or ameliorate its occurrence. Piper *et al.*'s (1987) framework takes a deductive approach derived from the five disciplines which have investigated fatigue (psychology, physiology, ergonomics, medicine and nursing). This framework often forms the theoretical base of current studies, and is used to guide the selection of variables for study and the structure of the data collection instruments (for example, Blesch *et al.*, 1991).

Conceptual frameworks developed for nursing have underpinned a number of studies, such as Orem's Theory of Self-Care and Levine's Conservation Model. Concepts derived from these frameworks have been related to the research questions or used as the organizing framework for the study, for example, the studies of Piper & Dodd (1991) and De Meyer (1991). Vincent (1992) chose to organize the multitude of factors suggested to be responsible for fatigue according to the energy model of Ryden (1977). Such models are useful, allowing us to organize the multiplicity of factors associated with fatigue in cancer. The framework could be used to assess the possible causes in this specific patient group.

The application of theoretical frameworks addressing specific components of fatigue may enhance understanding of fatigue in patients with cancer. Such an example is the work of Cimprich (1992a,b, 1993) who uses attentional theory to inform her research on attentional fatigue in women having surgery for breast cancer. More general models such as that proposed in relationship to morbidity of cancer patients by Thomas & Dodd (1992) could also be exploited within future study designs. The investigation of cancer-related fatigue currently is limited by a lack of well-developed theoretical frameworks that can be used to guide clinically relevant research. The inductive approach to theory development in this area tends to have been ignored or weighted in favour of the deductive approach, and the domains of fatigue open to study justified theoretically.

SUMMARY AND FUTURE RESEARCH DIRECTIONS

Looking at the research carefully it becomes evident that knowledge is insubstantial. A factor contributing to the lack of knowledge is a paucity of studies that address fatigue in cancer patients. For example, in the past 15 years only 11 nursing studies have been published in sufficient detail to allow critique that addresses fatigue as their primary focus. Three main areas must be addressed if our understanding of fatigue is to advance in a clinically relevant manner.

First, it is imperative that we develop valid and reliable ways of measuring the presence and intensity of fatigue. Research to date has many design and measurement problems. Typically, studies fail to include a control group, do not control for confounding variables and have restricted measurement to unidimensional scales with limited reliability and validity. For instance, many of the studies have employed a cross-sectional design with no control group. Consequently, there is no reliable way of ascertaining whether fatigue is any different for cancer patients than for healthy individuals or for patients undergoing treatment versus those who are not. With few exceptions most studies have failed to acquire an inception cohort of subjects. Studies employing a prospective design such as that by Pickard Holley (1991) are lacking. Lack of an inception cohort precludes controlling for the lapse of time since diagnosis or treatment. Patients should be identified at an early and uniform stage so that the clinical course of fatigue can be clearly identified.

Most studies are concerned with patients receiving treatment, but there is an absence of studies following the completion of therapy. Many are constrained by the cross-sectional approach. Cross-sectional study designs, in addition to heterogeneous samples of patients with a variety of tumour types, extents of disease, wide age range and varying treatment, introduce constraints under which research findings must be viewed as tentative. The number of patients involved in these studies is often small, limited to cancers of the breast, ovary, lung and the lymphomas. Future challenges lie in employing comparative and longitudinal prospective design to reveal patterns and implications of fatigue for the individual concerned and their family.

The measures used to evaluate fatigue have often been unidimensional and non-standardized, with limited validity and reliability testing. Fatigue has mostly been assessed by single items in general symptom checklists or mood rating scales. There are few specific instruments used in the cancer patient population. Here measures of fatigue are incorporated into instruments intended to measure broader aspects of patient functioning. A more comprehensive instrument, thoroughly tested for its psychometric properties, is not yet available.

Secondly, we must describe patient characteristics associated with fatigue. While several correlates have

been postulated, research to date has failed to verify consistent relationships between fatigue and other factors such as sleep disturbance, weight loss and psychological distress. Further work is needed between these and other correlates of fatigue. While there is evidence to suggest that fatigue interferes with the cancer patient's functional performance status, much of this work has been based on qualitative assessments with limited reliability and validity. It could be strengthened by the use of valid and reliable standardized scales measuring functional status. The outcome of fatigue has not been studied. Impact on quality of life, mobility, self-care, social isolation, role change, and family and caregiver fatigue, negative treatment and disease outcomes need to be explored in more detail.

Researchers and practitioners need to determine those interventions effective in reducing or eliminating fatigue. Studies are particularly needed in those areas where nursing could affect patient outcomes, and that are specific to different populations and situational contexts.

The research emphasis has undoubtedly focused on quantitative issues in the last two decades. We also need to document the fatigue experience from the patient's perspective. A broader view of a person's response to fatigue rather than the often narrow focus found in other disciplines should now be reflected in the research conducted. In-depth interviews of the fatigue experience are needed to clarify the multiple manifestations and meanings of fatigue.

Obviously, the methodological difficulties encountered in fatigue research must be overcome. Of equal interest, however, are the questions raised with respect to theoretical and conceptual problems. A more refined theoretical approach may broaden insight into fatigue. An explicit definition of the concept of fatigue is often lacking and a wide range of operationalizations is used; frequently, concepts such as malaise and weakness are used interchangeably as if they have the same meaning. Exploratory and descriptive work will culminate in concept clarification.

Little is known about the mechanisms that produce fatigue. Studies are required which utilize or take into account theoretical explanations for fatigue, and thus can validate, add to or refute factors proposed in various models and begin to provide an understanding of the mechanisms underlying fatigue in the cancer population.

In conclusion, fatigue is a major concern for the individual with cancer. Its prevalence and impact require that cancer care researchers devote more time to assessing this common phenomenon with methodologically sound studies. Serious research efforts must be concentrated in this area to provide an empirical base for clinical practice.

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The health diary: an examination of its use as a data collection method

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The health diary: an examination of its use as a data collection method

Use of a health diary has been common in nursing practice settings. Nurses have incorporated the diary as a means of helping clients to document their symptoms and factors which may have precipitated them, often with the aim of modifying particular health behaviours. To date there has been limited exploration of this tool in a nursing research context. Advantages and disadvantages associated with the diary when utilized as a research instrument in health settings are summarized and particular consideration is given to their use in nursing research with cancer patients. Features of the method such as completion and respondent co-operation, format and issues surrounding data analysis are considered. The advantages of this method warrant further exploration in nursing research, despite conflicting and insubstantial evidence regarding the feasibility, validity and reliability of specific kinds of information reported in a diary.

INTRODUCTION

Use of a health diary has been common in nursing practice settings. Nurses have incorporated the diary as a means of helping clients document their symptoms and factors which precipitated them, such as pain (McCaffery & Beebe 1989) and fatigue (Piper 1986), as well as recording such activities as medication use and dietary intake, often with the aim of modifying particular health behaviours.

To date there has been limited exploration of this tool in a nursing research context, yet the daily diary has been used sporadically as a data collection method in health services research since the 1950s. They have also been used to register daily social interactions, consumer expenditure and, in studies of food consumption, use of travel and time.

This present discussion will be limited to health diaries. There has been limited interest in the diary's unique characteristics as a research instrument (Kasl *et al.* 1975, Freer 1980a, Faithfull 1992), in particular when compared to morbidity and utilization surveys. The diaries referred to here are not those intimate journals people ordinarily keep for their own private purposes, although such documents have been employed in sociological and psychological research (Allport 1942). The term 'diary' is used here to refer to an annotated chronological record or log. Individuals are asked to maintain a record over time according to a set of instructions. The use of structured diaries is contested. Allport does not consider formally structured documentation as a true diary. Structuring, it is argued, forces the subject into a narrow view of their life events, decreasing spontaneity achieved with this format (Burgess 1984).

DATA COLLECTION WITH HEALTH DIARIES

To date health diaries have been used to describe an array of chronic and short-term illnesses and related

behaviours. The nature of data collected with the health diary has varied with the purpose of the study. For example, some diaries have elicited data regarding days on which the respondents experienced symptoms, days on which the respondents were unable to perform their usual activities and days on which individuals engaged in self-care, health-seeking activities, or took no action in response to symptoms (Kasl *et al.* 1975, Rakowski *et al.* 1988).

Freer (1980b) utilized health diaries over a period of 4 months in a study of the content and process of self-care practices of 24 women. The focus was on common everyday health problems. Freer felt the diary would yield more information than a retrospective health interview while the time frame permitted the investigation of recorded responses in response to perceived upsets of health. Diaries have been used to collect information about individual family members' health and illness behaviours. Individuals usually report data for themselves, although in some instances one person is asked to report for the entire family (Roghman & Haggerty 1972). Little is known about how children function as diary respondents, although their specific use by school-aged children has been reviewed by Butz & Alexander (1991).

The diary allows researchers to study health-seeking behaviour as a multi-faceted construct, not merely as a reflection of the uptake of health services. Diary-use allows documentation of symptoms and associated coping strategies by the individual or family experiencing them within their own frame of reference. Rakowski *et al.* (1988), as an example of diary usage in this area, documented the daily symptom experiences of older adults over a 2-week period and the actions they initiated. The facility to monitor symptom experience on a daily basis is an important consideration for investigators who wish to study health-behaviour decision-making and care-seeking actions.

Creation of indices

Rakowski *et al.* (1988) suggest that monitoring on a daily basis permits the creation of indices reflecting multiple points of data as they actually occur, rather than relying on reports of usual behaviour or responses to proposed scenarios. Recall techniques are likely to produce underreporting of short-term discomforts, nagging low-grade chronic conditions and minor bouts of ill health. Individuals may also retrospectively define past episodes as having been serious or not serious depending on what long-term effects remain, rather than based on the discomfort or disruption of routine that occurred at the time of the episode.

Lately, diaries have received interest in respect to data collection during a cancer patient's treatment (Geddes *et al.* 1990, Bleehen *et al.* 1991, Fayers *et al.* 1991, Fraser *et al.* 1993). In a series of Medical Research Council studies, which involved chemotherapy and radiotherapy for lung cancer, daily diary cards proved highly sensitive to day-to-day changes in symptoms (Jones *et al.* 1987, Bleehen *et al.* 1989, Bleehen *et al.* 1991, Fayers *et al.* 1991, Jones *et al.* 1987). The value of recording the intensity of symptoms and aspects of quality of life, taking account of the fluctuations which may be expected to occur during treatment and shortly following the cessation of treatment, has been recognized by these researchers.

Advantages of the method

Several advantages are associated with the use of a diary as a data source and as a data collection procedure because rich data can be obtained about an individual and the family health processes which surround health and illness and the decisions to seek help. The time sequence involved in the development of a symptom episode and the illness behaviour related to it can be documented, helping to determine the temporal relationship between the two events. A prime advantage is that participants can prospectively unfold a series of events and perceptions relevant to their subsequent action rather than rely on recall of past events (Allen *et al.* 1954, Roghman & Haggerty 1972). Diaries may be utilized for a number of differing purposes including (a) methodological studies comparing prospective diaries to other retrospective data collection sources, (b) aides-mémoires to improve recall of events in a later retrospective interview, and (c) a primary source of data (Verbrugge 1980).

Disadvantages of the method

Platt (1981) warns that diary sources should not be viewed uncritically. Disadvantages associated with this method include: expense in terms of interviewer time needed for instruction, follow up and coding of the results, elimination of those participants who cannot read or write or those who choose to not keep the diary, inability of the researcher to immediately probe for additional data beyond that provided and linguistic biases dependent on the individual's education and literary background. Another important source of bias associated with this method occurs when an investigator studying families requests one member to report for others. Kosa *et*

Table 1 Some reported advantages and disadvantages when utilizing diaries as research tools

Advantages
Produce rich data regarding processes used to promote health and cope with illness in individuals over time
Support dynamic as well as static analysis
Does not rely on retrospective reflection, thus reduces recall error
Can be descriptive and intimate
High levels of reporting achieved when compared to retrospective interviews
A series of events can be documented and examined for causal relationships
Disadvantages
Time required to instruct about tool and follow up
Bias in that excludes participants who canot read or write
Inability of the interviewer to probe for further information, must be taken at face value
Dependent on the motivation of participant
Crucial data may be omitted/skipped
Conditioning effects may occur
Survey costs are high
Data collection, processing and analysis may be complex

al. (1967) mentions the possibility of mechanisms of censorship operating where respondents only record those symptoms which meet certain minimum requirements of severity and duration. Representativeness of the sample may suffer due to non-participation, potential subjects may decline to commence the diary and subjects may skip days or suspend diary completion prior to the intended end of data collection.

Summary

The advantages and disadvantages associated with the diary when utilized as a research instrument in health settings are summarized in Table 1. Verbrugge (1984) counters many of the persistent arguments levelled against diaries as research instruments, which have been mentioned above, and offers empirical evidence and solutions to many of the problems encountered. The researcher should carefully consider such issues prior to embarking on any study which will utilize this method.

FEATURES OF THE DIARY AS A RESEARCH INSTRUMENT

Compliance and respondent co-operation

This type of data collection method obviously demands more time and effort on the part of the respondent than, for example, single interviews, and constitutes a clerical task to which people will respond with differing levels of skill and enthusiasm. The length of the data collection period for which diaries have been maintained spans from anything from 1 to 2 weeks (Kasl *et al.* 1975) to over 1 year (Freer 1980b). Several studies have used strategies such as remuneration, follow-up telephone calls and follow-up interviews and visits to collect diaries and checks for completeness. Financial remuneration may not be important in influencing the decision to participate, but probably influences commitment to complete the diary.

Norman *et al.* (1982) argue that there appears to be good reason to limit the total duration of diary usage. Initial compliance may be high amongst those who participate, but there is a consistent drop in the reporting of incidents with the passage of time. Bleehen *et al.* (1989), reporting on the Medical Research Council Lung Cancer Working Party experience with daily diary cards, revealed very poor compliance in this group. Specific centres contributed to the low rate. No reasons are offered. However, little effort appears to have been devoted to maintaining the sample and the research team expected patients to complete cards from admission until imminent death.

Roghman & Haggerty (1972) noted a decline in reporting during stressful events, and this may represent either a waning motivation to record data as time progresses, or may indicate that the participants' perceptions as to what constituted such an event changed as diary completion progressed. Mooney (1962) has attributed this to fatigue, a lack of willingness to complete the diaries in the same detail as time passes. Norman's solution to this problem was to ask respondents to complete a randomly selected 3-day block every 2 weeks. Additionally, telephone contact was made 48 hours prior to the scheduled day of completion and lottery tickets were given. This combination of strategies maintained a high compliance in a study conducted over 2 years in a sample of over 400 individuals.

Verbrugge (1984) considers attrition, task performance and conditioning effects in some detail in relationship to the general population. He produces recommendations based on the results of the Detroit Health Study about staff activities, diary format and field procedures which would result in retention of a sample, improvement in record quality and reduction in reactivity to the study.

Analysis of sample members with complete diaries may reveal particular characteristics. Carp & Carp (1981) revealed that attrition related to diary-keeping resulted in

under-representation of certain groups (e.g. low income, little education, minority ethnicity and poor health).

Format

Diaries are constructed according to one of two formats:

1 as a journal, where all health events are entered on the same page for each day,
2 as a ledger, where separate pages are used for different types of events, e.g. medication use and visits to the doctor.

Freer (1980a) provides useful information on the organization, planning and management of a health diary study: for example, it should be established that the respondent interprets the question in the same way as the organizer. Unstructured diary sheets in health research have been found to yield disappointing results. Structuring the situation as much as possible allows even the less-articulate respondents to provide daily information, for example, by ticking boxes. The respondents should be able to complete the diary in less than 5 minutes. However, little is known about the technical aspects of design which aid respondents. Its salience may lead to high co-operation in those most affected by the problem under investigation.

Reliability and validity

Diary strategies have been used relatively rarely, and little is known about their psychometric properties. However, as the method does not require the respondent to recall past events, it seems likely to provide more valid and reliable descriptions of minor and frequent events than the interview approach (Allen *et al.* 1954). In general, diary errors usually involve incorrect or missing data, whereas interview error involves the participants telescoping events into smaller time periods (Roghman & Haggerty 1972). These authors concluded that the diary is a more valid approach to collecting data regarding the use of health surveys than interviews, particularly for time sequence data involving illness behaviour. The possibility of conditioning effects such as sensitization, fatique and mechanical response sets are discussed in the literature (Verbrugge 1980).

Carp & Carp (1981) analysed five sets of data to assess the reliability, validity and generalizability of diary data. Results suggested that scores obtained from 1-week diaries had satisfactory construct validity and that for salient activities they were less subject to retrospective bias than interview data.

The quality of data provided seems closely related to the effect devoted by staff in encouraging diary-keepers to maintain them, reducing missed pages, missing items and ambiguous entries. Validity is difficult to assess, but one strategy is commonly used to assess validity of self-reported health events: recordings may be compared with clinical and hospital records of health care visits (Roghman & Haggerty 1972), thus producing an estimate of criterion validity although this is only possible for health events that involve medical care. Interviewing respondents about events recorded in a diary within a given time frame can also be attempted. When the rates of events obtained by interview versus diary have been compared for groups of individuals outcomes have been similar.

Reliability and validity estimates have been attempted by using different instruments to measure the same categories of events of concern to the researcher; for example, the Follick *et al.* (1984) study. Geddes *et al.* (1990) also used this approach when studying the utility of the daily diary card to study quality of life in patients receiving a randomized trial of chemotherapy in small cell lung cancer. Comparison was made between the diary card, nurse ratings using the card, the European Organization For Research and Training in Cancer questionnaire (Aaronsen 1993) and the Spitzer quality of life index (Spitzer *et al.* 1981). These comparisons revealed expected convergent and divergent validity and demonstrated sensitivity of the diary card to short-term changes compared with the other measures.

This strategy was also used by Woods (1981). The criteria used for validation of the health diary included a recognized index of mental health, the Cornell Medical Index M–R scale (Brodman *et al.* 1956), and the individual's assessment of self-perceived health. The data obtained from family health diaries were compared with scores and self-ratings obtained during interviews. Symptoms reported in the diary were only weakly correlated with the scores from the Cornell Medical Index M–R scale and poorly correlated with a self-perceived health rating. This author concluded that it was better suited to the documentation of asymptomatic days, and thus more useful for studying disease or problem-free periods rather than documenting specific symptoms.

This study demonstrated conflicting utility of the diary as a nursing research instrument. Many of the advantages noted by previous researchers were supported but a number of disadvantages were apparent. It appeared to be a weak measure of mental ill health or poor health on this occasion, but strong arguments to explain why this may have occurred were suggested by the author.

Data analysis

Diaries provide a continuous stream of daily data from each individual. This holds enormous analytical potential for the analysis of variations over the entire diary period and day-by-day. It makes possible both individual-level and aggregated analysis with the use of multiple perspectives, investigating changes both within and across groups. The objectives of analysis invariably involve the summary of patterns and detecting changes over time, comparing patterns of variables in differing groups for similarity or divergence with time. The *individual* and the *day* can be used as the unit of analysis.

Data collection and processing are not intrinsically more complex. However, these activities may be more labour-intensive than for other survey procedures, and the data more difficult to analyse, partly because they require new analytical perspectives and partly because 'They strain the capacity of statistical techniques now available' (Verbrugge 1980). Abraham & Neundorfer (1990) feel that, currently, the statistical methods utilized in nursing research chiefly consider data as cross-sectional, 'capturing a state as it exists at one point in time'. This concept of statistical analysis is not always suitable for studying change over time (Gabriel & Dush 1988).

Aim of analysis

The analysis of health diary data has been examined in detail by only a limited number of writers; for example, Eckenrode (1984), Fayers & Jones (1983), Machin *et al.* (1987). Verbrugge & Balaban (1989), through recourse to a completed diary study, identified techniques for visual and statistical analysis and concluded with a useful discussion of longitudinal data, noting the special features of such a data set and what to expect and learn from it. The aim of such analysis is summarized as 'taking advantage of the data's richness, with minimal sacrifice of detail. Thus, though the initial challenge is to collect the data at all, the ensuing one is to summarise them in a coherent and usable manner'. Missing data inevitably lead to problems in conducting statistical analysis, and as yet there have been few guidelines in the literature of how to deal with this (Fayers & Jones 1983).

The utilization of time-series analysis may be of value. Metzeger & Schultz (1982) have described the potential contribution of time-series studies to nursing research. A time series is involved when there are multiple observations over time (Cook & Campbell 1979). Time-series analysis refers to the statistical models for the analysis of a time series. This approach to data analysis allows the sophisticated longitudinal analysis of data from time $t_o \ldots t_n$, and generates a statistical model to explain such data and predict future values. It facilitates the incorporation of all data collected sequentially over the chosen time period. The salient feature of time series analysis lies in the fact that successive observations are not usually independent, so analysis must take into account the chronological order of observations. This technique provides the tools essential for analysing unique behaviour fluctuations through time and a framework for predicting future change in that individual's behaviour (Metzeger & Schultz 1982).

DIARIES IN NURSING RESEARCH WITH CANCER PATIENTS

There has been little exploration of this tool in a nursing-research context. The following studies highlight the use of diaries with a cancer-patient population.

Oleske *et al.* (1990) discuss the rationale and methodology of diary data collection with an ill population focusing on an experience with a sample of cancer patients receiving domicillary nursing care. Diary recordings were obtained and evaluated in order to gain insight into the nature and magnitude of health problems encountered in the home by individuals with cancer. A monetary incentive was offered. It was noted that the sheer volume of patient recording made it apparent that the issue of respondent burden need not be of great concern with the use of such an instrument. Oral comments given by diary keepers to research assistants, when calling to instruct the respondents, indicated that they found keeping diaries a helpful outlet. Data collection therefore appears feasible for longitudinal research of older individuals with a chronic condition such as cancer.

In this study, less that 5% of the sample were receiving active cancer treatment during data collection. In general, the researchers felt that diaries could be useful data collection methods in measuring the quality of life over time with chronically ill elderly individuals. Utilizing the diary method of data collection can assist in identifying the subtleties of health-problem variation among people with advanced cancer and also may pave the way towards developing new strategies for improving quality of life.

The diary as a record of health-related events was used by Frank-Stromborg (1986) to investigate the health-promotion behaviours in the ambulatory cancer patient. This approach to data collection was selected because of its suitability for symptom disability and health action reporting. The researcher examined cancer clients' self-care and health-promoting activities. The diary employed

daily ratings, closed responses and open-ended questions in attempts to evaluate what ambulatory cancer clients do to feel better. The author claimed that a health diary would result in high levels of reporting, sensitivity to detail, reduction of memory recall bias and the ability accurately to reflect individual daily reports of health and health actions.

Dodd initiated a series of studies to examine the self-care practices of chemotherapy and radiotherapy patients through which she developed a self-care behaviour log (Dodd 1984b,c, 1987, 1988a,b, 1990). The studies were published in sequence and explored differing aspects of a general focus concerned with determining the nature and frequency of self-care behaviours initiated to alleviate side-effects. One of the most recently reported (Dodd 1988b) studies intended to replicate and extend previous research (Dodd, 1982a,b, 1983, 1984a), incorporating earlier recommendations, and attending to some of the previous methodological weaknesses, hoping to provide further understanding of the frequency and nature of self-care behaviours and influencing factors. The inclusion of a self-care behaviour log, rather than a retrospective questionnaire to eliminate reliance on recall, is of relevance to the present discussion.

Experience of side-effects

In the log patients record each side-effect as it is experienced, indicating the date of onset. They also record the severity and distress experienced (two 5-point scales), the self-care behaviour undertaken to alleviate the side-effect, perceptions of the effectiveness of each self-care behaviour (rated on a third 5-point scale) and their sources of information for each self-care behaviour. Versions of this log have been utilized in the study of preventive self-care in relation to potential side-effects (Dodd 1984c), and in the evaluation of the efficacy of providing proactive information on self-care performance in patients receiving radiotherapy and chemotherapy (Dodd 1987, Dodd 1988a).

Unfortunately there is little discussion on aspects associated with compliance and missing data due to toxicity of side-effects. In one of the later studies (Musci & Dodd 1990) mention is made of the fact that 38 out of 80 families who were approached did not complete the study. Reasons for non-completion included complications of treatment or disease, incomplete questionnaires and death of the patient. Most patients were hospitalized for complications resulting from side-effects at some point in time.

Data analysis in all studies is limited. It is invariably aggregated to produce various ratios of the self-care behaviour log, quantifying the frequency, effectiveness of self-care activity, and overall management of the experienced side-effects. Time as a variable is only considered when determining the relationship of the duration of experienced side-effects to initiation of self-care behaviours (delay in initiating behaviours). The reliability of the log could benefit from further testing and attention to measures to explore validity, but the utility has been demonstrated in enabling the self-report of symptoms.

This approach has been selected by the present author in the development of a simplified method of determining fatigue and selected factors postulated to effect this phenomenon in cancer patients receiving chemotherapy. Of primary importance has been the development of a patient self-report instrument that is comprehensive and robust while also being of sufficient brevity to be of practical use. As a research tool this simple, rapid method could be useful in assessing the effectiveness of nursing interventions in these stressed and sick individuals. The diary is designed to elicit information concerning the intensity, severity and distress associated with fatigue and patient-initiated coping strategies undertaken to manage the problem in the previous 24-hour period.

Elements

The diary consists of a number of elements:

1. Four visual analogue scales representing various dimensions of the fatigue experience and ticked boxes to confirm the presence of fatigue during certain periods of the day.
2. A record for the patient to make explicit any actions performed in relationship to the relief of fatigue, the effectiveness of such actions (rated on a 4-point scale) and the source of idea for such actions. This portion of the diary is a self-report instrument adapted from the questionnaire and log of Dodd (Dodd 1982a, 1983) designed to elicit information concerning self-care actions taken by patients in a previous 24-hour period.
3. Open-ended items eliciting ideas about the contributory causes of fatique and any other symptoms experienced that day.

A sheet from the diary serves to illustrate the format in the Appendix. It was felt that daily completion over a period of approximately 1 month would not place an

undue burden on the participants, even though the respondent might be suffering from fatigue. No more than 5–10 minutes is required to complete the diary each day. A copy of the instructions for diary completion are bound inside the front cover. This includes a sample recording of the method of completion. Participants do not appear to find the task onerous or difficult; on the contrary many participants find that it is useful and provides solace. Some respondents are willing to complete serial administrations of the instrument over periods up to 28 days. Patients often welcome the opportunity to report their experiences and concerns even within the confines of a formal research investigation.

CONCLUSION

Diaries seem to be as flexible and, in principle, as widely applicable research instruments as questionnaires and interviews in the circumstances described above. Issues relate not only to their feasibility, but their relatively high cost, the greater degree of co-operation required from the respondent, and the vastly increased work involved in the complete analysis of all the data collected. Although used infrequently in nursing-research studies with patients who are undergoing active treatment and potentially unwell, the present researcher considers the diary method a potentially efficient and sensitive tool with which to reveal information.

Research predominates in nursing which utilizes cross-sectional design or data collection at spaced predetermined intervals. There are many assumptions made as to what occurs in the intervals between these measurements. Researchers risk missing important changes during such intervals, including declines in health status which are later reversed. Longitudinal design has relevance for nursing research since the phenomena nursing deals with, individual human responses to health status and/or problems, often involve determining patterns, rather than isolated occurrence (Barnard *et al.* 1987). The diary is a valuable strategy for detecting change in individuals or groups over time but as a data collection method in longitudinal designs it has been exploited very little.

Studies should be designed which examine ways in which the limitations of this method can be compensated for and its strengths capitalized upon. Woods (1981) developed criteria to guide researchers as to the circumstances when selection of this method alone, or in tandem with other methods, would be fruitful. Linking diary data with other methods should be explored as this is considered a potentially valuable approach (Zimmerman & Wieder 1977, Platt 1981). Continued exploration of the health diary as an instrument for nursing research could bring rich rewards.

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APPENDIX: SAMPLE SHEET FROM THE DIARY*

Daily Fatigue Diary

1. Did you feel fatigued today? Please tick the appropriate box [Yes] [No]

   If the answer is *yes* please complete the items below by placing a mark through the line at the point which most closely resembles how you have felt today where this is required.
   If you answered *no*, there is no need to complete the diary today.

2. To what extent did you experience fatigue today?

   No fatigue _____ A great deal of fatigue

3. To what degree did your fatigue cause you distress today?

   No distress _____ A great deal of distress

4. To what degree did the fatigue you felt today prevent you or interfere with your ability to carry out your daily activities and chores?

   Not at all _____ A great deal

5. To what degree did the fatigue you felt today prevent you from doing the things you enjoy, e.g. visiting friends, going out, pursuing your hobbies?

   Not at all _____ A great deal

6. Please could you tick the boxes which indicate the periods of the day when you felt fatigued.
   If you felt fatigued on different occasions, you can tick more than one box.

   [early morning] [late morning] [early afternoon] [late afternoon]
   [early evening] [late evening]

Daily Fatigue Diary Continued

7. Did you perform any actions which you hoped would relieve your fatigue today?

Please tick the appropriate box [Yes] [No]

If you answered *yes*, please complete the section below:

	Action taken	Effectiveness of action in relieving fatique (please tick a box)				Source of idea for action
		not relieved	partly relieved	nearly completely relieved	completely relieved	
a)	_____	[1]	[2]	[3]	[4]	_____
b)	_____	[1]	[2]	[3]	[4]	_____
c)	_____	[1]	[2]	[3]	[4]	_____
d)	_____	[1]	[2]	[3]	[4]	_____

8. When feeling fatigued today, what do you believe contributed to or caused your fatigue?

_____

_____

9. Did you experience any other symptoms or problems today? Please tick the appropriate box.

[Yes] Please describe _____

_____

[No]

*Part 7 is adapted from Dodd (1982a, 1983).